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CASE REPORT

Intravenous immunoglobulin replacement therapy to prevent pulmonary infection in a patient with Good's syndrome

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Good's syndrome is an acquired immunodeficiency state associated with thymoma and characterized by recurrent pulmonary infections. We describe a 67-year-old woman who presented with respiratory symptoms caused by concomitant disseminated cytomegalovirus infection and *Pneumocystis jiroveci* pneumonia 38 months after thymectomy for a thymoma. Immunologic analysis revealed hypogammaglobulinemia with absent B-cell population as demonstrated by flow cytometry, consistent with Good's syndrome. Following treatment with sulfamethoxazole/trimethoprim and ganciclovir, the patient improved with resolution of her respiratory symptoms. However, the patient subsequently experienced additional infections, necessitating additional subsequent hospital admissions. During the last admission, intravenous immunoglobulin (IVIG) replacement therapy was initiated and continued after discharge.

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Infection has been prevented for one year after beginning IVIG replacement therapy. This case reveals that in patients with combined humoral and cell-mediated immune deficiency, concomitant infection with different pathogens is not unusual, and immediate specific therapy is important. Periodic IVIG infusion, to maintain adequate Ig levels, is recommended.

Introduction

Patients with thymoma can experience various forms of paraneoplastic syndromes. The three most common are myasthenia gravis, pure red cell aplasia, and hypogammaglobulinemia.[1] Hypogammaglobulinemia occurs in 3–6% of patients with thymoma. This association, first reported by Robert Good and colleagues in 1954, is referred to as Good's syndrome,[2] and is characterized by low to absent B-cell numbers in the peripheral blood, hypogammaglobulinemia, and defects in cell-mediated immunity, resulting in recurrent infection by various microbial pathogens. We herein present the successful treatment of a patient with Good's syndrome infected with concomitant disseminated cytomegalovirus (CMV) infection and *Pneumocystis jiroveci* pneumonia (PJP), and discuss the use of prophylactic immunoglobulin replacement therapy for such patients.

Case report

A 67-year-old woman was admitted to our hospital because of dyspnea and fever for 1 day. She had been in good health until 6 years earlier, when she started to experience a refractory productive cough. At that time, chest computed tomography performed showed a heterogeneous soft-tissue mass (approximately 13.8 × 9.5 × 6.0 cm) in the prevascular space of the left anterior mediastinum, consistent with a thymoma (Fig. 1). Thymectomy was performed through a median sternotomy. Histopathological diagnosis of the resected tumor was consistent with a thymoma, type AB, based on the World Health Organization classification. The tumor had infiltrated into, but not through, the capsule. She received adjuvant radiation therapy after the operation. Following completion of the therapy, the patient remained in good health until 3 months after the operation, when she was admitted for PJP and herpes zoster infection of the skin. She was subsequently admitted to the hospital twice due to sepsis by *Streptococcus pneumoniae* and CMV infection on the 27th and 35th months. Thirty-eight months after thymectomy, she was admitted again. Physical examination on admission revealed a fever of 39.6 °C, pulse rate 116 bpm, blood pressure 92/60, respiratory rate 28, and SpO_2: 96% under 3 L/min nasal canula, moist skin, and coarse crackles in the bilateral lower chest. The leukocyte count was 13,240/μL with 86% neutrophils, 9% bands, a platelet count of 230,000/μL, and a C-reactive protein level of 10.38 mg/dL. Arterial blood gas showed a pH of 7.39, $PaCO_2$ of 44 mmHg, PaO_2 of 75 mmHg, and SaO_2 of 96% while breathing 60% supplemental oxygen via a face mask. Chest computed tomography on admission showed diffuse reticulonodular/ground-glass opacities and interstitial infiltration bilaterally, suggestive of chronic interstitial lung disease with superimposed acute infection (Fig. 2). Broad-spectrum antibiotic treatment with piperacillin/tazobactam was administered. Since her medical history indicated repeated episodes of pneumonia with various pathogens, including opportunistic pathogens, the immune status of the patient was assessed during the hospitalization. Significantly decreased levels of IgG (375 mg/dL), IgM (5 mg/dL), IgA (38 mg/dL), and IgE (<5 IU/mL) were noted. Evaluation of peripheral lymphocytes by flow cytometry revealed the lack of B-cell lineage (negative for CD19 and positive for CD3) with reversed T helper to suppressor ratio (0.32). CD4 T-cell number was 452/μL. Antibody to human immunodeficiency virus (HIV) was negative. Combined with the previous thymoma history and immune abnormality, these results established a diagnosis of Good's syndrome.

Despite treatment with broad-spectrum antibiotics, the fever persisted with little improvement of the symptoms. Polymerase chain reaction (PCR) using real-time *TaqMan* PCR on blood, urine, and sputum specimens were positive for CMV, consistent with a diagnosis of disseminated CMV infection. The concomitant diagnosis of PJP was established by a positive sputum PCR for *P. jiroveci*. Sulfamethoxazole/trimethoprim and ganciclovir were prescribed accordingly, and symptoms improved after treatment. The patient was then discharged in stable condition, but

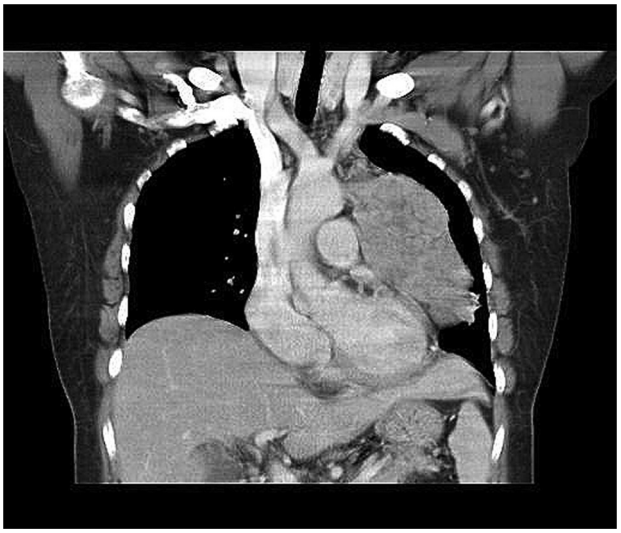

Figure 1. A mass (about 13.8 × 9.5 × 6.0 cm) in the prevascular space of the left anterior mediastinum consistent with a thymoma.