Good’s Syndrome Patients Hospitalized for Infections

A Single-Center Retrospective Study

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Abstract: Good’s syndrome (GS) is a rare combination of thymoma and hypogammaglobulinemia, resulting in immunodeficiency. Patients with GS are highly susceptible to bacterial infection, particularly encapsulated bacterial infection in upper and lower respiratory tracts. Good’s syndrome patients with moderate-to-severe infection are often hospitalized. Clinical features of GS patients remain to be characterized. Patients with the discharge diagnosis of GS and simultaneous infection from Peking Union Medical College Hospital between January 2001 and July 2015 were retrospectively analyzed.

Among 14 hospitalized GS patients, 12 of them were admitted for severe infections. Mean patient age was 56.7 ± 10.1 years. Average concentrations of serum IgG, IgA, and IgM were 2.3 ± 1.9 g/L, 0.28 ± 0.28 g/L, and 0.06 ± 0.07 g/L, respectively. Respiratory and intestinal tracts were the most common sites for infection, which occurred in 7 and 4 patients, respectively. Pathogens identified in 10 patients included cytomegalovirus in 5 patients, Pneumocystis jiroveci, Clostridium difficile in 2 patients, Klebsiella pneumonia in 2 patients, and Streptococcus pneumonia and Hemophilus influenza in 1 patient. Ten patients were treated with antibiotics and immunoglobulin replacement. Only 1 patient who was on immunosuppressant therapy died from P. jiroveci pneumonia.

Infection was the most frequent cause for hospitalization of GS patients. Both respiratory and intestinal tracts were the most common sites of infection. Cytomegalovirus and P. jiroveci represented 2 common opportunistic pathogens isolated from hospitalized GS patients with infections.

METHODS

The medical files of patients who were hospitalized at Peking Union Medical College Hospital from January 2001 to July 2015 were searched for the discharge diagnosis of “Good’s syndrome.” Only GS patients with infections were included in this retrospective study. The following data were retrieved for analysis: age, sex, clinical symptoms, laboratory findings, sites of infection, treatment, and outcomes. Informed consent was waived because of the retrospective nature of this study. The study was approved by the Ethical Committee of Peking Union Medical College Hospital.

Good’s syndrome is defined as following: (1) the presence of thymoma, confirmed by chest computed tomography and/or pathology; and (2) hypogammaglobulinemia, defined as serum immunoglobulin G (IgG) < 5 g/L, and/or immunoglobulin A (IgA) < 0.7 g/L, and/or immunoglobulin M (IgM) < 0.4 g/L.

An infection was diagnosed when clinical manifestations indicated infection (fever, cough, sputum, diarrhea, etc) and corresponding pathogens were identified. The infection was also diagnosed if clinical manifestations for infections were unequivocal and the treatment aiming at the infection was effective even no pathogen was isolated. Quantitative data were expressed as mean value ± standard deviation, and qualitative results were described as percentage.

RESULTS

A total of 14 patients with Good’s syndrome were initially identified during this period. Two patients were excluded because of no infection associated with their hospitalization, and 12 patients were eligible for this study. All of 12 patients were hospitalized for moderate to severe infections. The clinical characteristics are summarized in Table 1. Female patients accounted to three-fourths of 12 patients, and the patient age was ranged from 38 to 70 years (mean age 56.7 ± 10.1 years). The thymoma was histologically confirmed in all patients and resected in 10 of them. The histological classification of...
| Gender | Age (Years) | Type of Thymoma | Clinical Symptoms of Infection | Sites of Infection | B lymphocyte Count (Cells/μL) | Treatment | Outcome | Pathogen | Comorbidity | Treatment | Outcome |
|--------|-------------|-----------------|-------------------------------|-------------------|-----------------------------|-----------|---------|----------|------------|-----------|---------|
| Female | 38          | Type A          | Fever, joint pain             | Upper respiratory tract | 0.07 g/L, 0.28 +, 0.06 +   | None      | None   | None    | None       | None      | None   |
| Female | 56          | Unknown         | Fever, cough, dyspnea         | Lung               | 0.67                        | Leukopenia| Remission| CMV     | None       | Leukopenia| Remission|
| Female | 68          | Benign          | Fever, cough, dyspnea         | Lung               | 2.83                        | IVIG + antibiotics | Remission| K. pneumonia | None      | IVIG + antibiotics | Remission|
| Female | 47          | Type A          | Fever, cough, dyspnea         | Brain              | <0.33                       | None      | None   | None    | None       | None      | None   |
| Female | 63          | Malignant       | Fever, cough, dyspnea         | Upper respiratory tract | 6.69                        | IVIG      | Remission| CMV     | None       | IVIG + antibiotics | Remission|
| Male   | 67          | Type A          | Ferry, cough, dyspnea         | Intestinal tract   | 1.53                        | Antibiotics | Remission| CMV     | None       | IVIG + antibiotics | Remission|
| Female | 61          | Unknown         | Ferry, cough, dyspnea         | Lung               | 3.15                        | None      | None   | CMV     | None       | IVIG + antibiotics | Remission|
| Female | 63          | Mixed           | Fever, cough, dyspnea         | Intestinal tract   | 1.8                         | HA         | Remission| CMV     | None       | IVIG + antibiotics | Remission|
| Female | 37          | Malignant       | Fever, cough, dyspnea         | Lung               | 3.53                        | None      | None   | CMV     | None       | IVIG + antibiotics | Remission|
| Female | 57          | Type AB         | Fever, cough, dyspnea         | Lung               | 3.53                        | None      | None   | CMV     | None       | IVIG + antibiotics | Remission|

### TABLE 1. Clinical Characteristics of Good’s Syndrome Patients Hospitalized for Infections

| Age (Years) | Type of Thymoma | Clinical Symptoms of Infection | Sites of Infection | B lymphocyte Count (Cells/μL) | Treatment | Outcome | Pathogen | Comorbidity | Treatment | Outcome |
|-------------|-----------------|-------------------------------|-------------------|-----------------------------|-----------|---------|----------|------------|-----------|---------|
| Female      | 38              | Type A                        | Fever, joint pain  | Upper respiratory tract     | 0.07 g/L  | None    | None     | None       | None      | None    |
| Female      | 56              | Unknown                       | Fever, cough, dyspnea | Lung                    | 0.67      | Leukopenia| Remission| CMV       | None      | IVIG + antibiotics |
| Female      | 68              | Benign                        | Fever, cough, dyspnea | Lung                   | 2.83      | None    | IVIG     | K. pneumonia | None      | IVIG + antibiotics |
| Female      | 47              | Type A                        | Fever, cough, dyspnea | Brain                  | <0.33     | None    | IVIG + antibiotics | None       | None      | None    |
| Female      | 63              | Malignant                     | Fever, cough, dyspnea | Upper respiratory tract   | 6.69      | IVIG    | Remission| CMV       | None      | IVIG + antibiotics |
| Male        | 67              | Type A                        | Ferry, cough, dyspnea | Intestinal tract         | 1.53      | Antibiotics| Remission| CMV       | None      | IVIG + antibiotics |
| Female      | 61              | Mixed                         | Ferry, cough, dyspnea | Lung                   | 3.15      | HA      | Remission| CMV       | None      | IVIG + antibiotics |
| Female      | 37              | Malignant                     | Ferry, cough, dyspnea | Lung                   | 3.53      | None    | IVIG + antibiotics | CMV       | None      | IVIG + antibiotics |

**DISCUSSION**

To the best of our knowledge, this study presented the largest series of GS patients who were complicated by infections in a single center. We revealed several interesting findings: (1) infections were the most frequent cause for hospitalization of GS patients; (2) respiratory and intestinal tracts were the most common sites of infection in hospitalized GS patients; (3) opportunistic pathogens including CMV and *P. jirovecii* were commonly detected in hospitalized GS patients with infections.

Both our study and the literature showed that GS had a peak incidence of infection in the 5th and 6th decade. A systemic review demonstrated that 83.3% of GS patients caught infections. In this study, the infections were identified in 85.7% of the hospitalized GS patients, suggesting that infection was the most frequent cause for hospitalization of GS patients. This finding implies that GS should be suspected in a thymoma patient with recurrent infections.

It has been reported that upper and lower respiratory tracts were the most common sites of infection in GS patients. Upper respiratory tract infection and superficial fungal infection were precluded in this study because they generally would not be hospitalized. Pulmonary infection was noted in 58.3% of patients in this study. However, in GS patients who were regularly followed for a long period of time, as high as 85.7% of patients had at least 1 episode of pneumonia. A systematic review showed that diarrhea occurred in 31.8% of GS patients, but only 11.4% of patients were infected. A higher percentage (58.3%) of patients with diarrhea was detected in this study, and 33.3% of them had infectious diarrhea, demonstrating that the intestinal tract is another frequent site of infection in GS patients.

Bacteria, especially encapsulated bacteria including *S. pneumoniae*, *H. influenzae*, *K. pneumoniae*, are the most important pathogens in infected GS patients. Similar pathogens were identified in our study. Recurrent bacterial infection in GS patients most likely reflects the IgG deficiency, the part of problems with GS.
Different from common variable immunodeficiency (CVID),6,7 cell-mediated immunodeficiency is a common manifestation in GS patients. CD4+ T lymphocyte count was decreased in all patients and was <400 cells/μL in 58.3% of patients. Cell-mediated immunodeficiency explains why GS has a poorer prognosis than CVID.11,12 Although pathogenic bacterium is the most common pathogen in all GS patients,5 opportunistic pathogens associated with cell-mediated immunodeficiency including CMV (41.7%) and P. jiroveci (16.7%), frequently caused opportunistic infections in hospitalized GS patients in this study. CMV often appeared to cause intestinal infection, and P. jiroveci led to pulmonary infection.

Thymoma features with autoimmunity, and 32.7% to >50% of patients with thymoma exhibited autoimmune manifestations.13,14 Pure red cell aplasia (PRCA) was the most common autoimmune complication associated with GS7 as shown by this cohort. Leukopenia is also a common finding in GS patients,15 as was detected in 33.3% of patients in this study. Leukopenia is also a common finding in GS patients,15 as was detected in 33.3% of patients in this study. Although myasthenia gravis (MG) is a common comorbidity of thymoma, it is relatively rare in GS patients. In fact, none of our GS patients exhibited MG symptoms, which was consistent with another GS series.10

Thymectomy is usually recommended in all patients with thymoma to prevent locally invasive growth and metastasis of tumor cells.16,17 It usually favorably impacts associated conditions such as PRCA and MG. However, the thymectomy is usually ineffective in improving immunodeficiency in GS patients, and it might worsen hypogammaglobulinemia in rare cases.18 Immunoglobulin replacement has been used to maintain appropriate serum IgG concentration to reduce infection.5,8,19 In this study, 83.3% of GS patients were infected and they received immunoglobulin replacement therapy in addition to antibiotics, resulting in clearance of infections in the majority of patients. Therefore, we recommend immunoglobulin replacement as standard therapy in all hospitalized GS patients with infections. The only patient who died in this study was an old woman who developed PRCA. She was on corticosteroid and immunosuppressant therapy when she caught pulmonary infection with P. jiroveci.20 In our opinion, the immunosuppressive drugs contributed more to her death than GS itself.

Because GS is a rare disease, the value of this study is limited by relatively small number of enrolled patients. Additionally, there are no definite criteria for hospitalization of GS patients, which may have resulted in biased findings by this study. Nonetheless, this study excluded many mild or less important infections, which highlighted important infections in GS patients that should be managed timely and carefully.

In conclusion, infections are a common manifestation in GS patients and are the most frequent cause for hospitalization. Beside the pathogenic bacteria, opportunistic pathogens including CMV and P. jiroveci represent frequent causes for infection. We recommend a combination of antibiotics with immunoglobulin replacement as standard therapy for hospitalized GS patients with infections.

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