Infect Dis Ther (2014) 3:333–337
DOI 10.1007/s40121-014-0045-7

CASE REPORT

A Bad Case of Good's Syndrome

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Received: July 14, 2014 / Published online: October 7, 2014

ABSTRACT

Good's syndrome is a relatively rare immunodeficiency condition that presents in the fourth or fifth decade of life and is defined by hypogammaglobulinemia in the setting of a thymoma. The humoral defect may be severe enough to cause an absence in B cells, with a consequent recurrence of sinopulmonary disease, chronic non-infectious diarrhea and opportunistic infections. The prognosis in patients with Good's syndrome appears to be worse than in those with X-linked agammaglobulinemia (XLA) and common variable immune deficiency (CVID). There have only been three cases of Good's syndrome associated with mycobacterium, and only one case with a cavitary lesion in the lungs. We present here a unique case of Good's syndrome with a non-mycobacterial cavitary lesion.

Keywords: Cavitary lesion; Good's syndrome; Hypogammaglobulinemia; Intravenous immunoglobulin; IVIG; Immunodeficiency; Thymoma; *Pneumocystis jiroveci*

Electronic supplementary material The online version of this article (doi:10.1007/s40121-014-0045-7) contains supplementary material, which is available to authorized users.

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INTRODUCTION

Good's syndrome is a relatively rare immunodeficiency condition that presents in the fourth or fifth decade of life and is defined by hypogammaglobulinemia in the setting of a thymoma [1]. The humoral defect may be severe enough to cause an absence in B cells, with a consequent recurrence of sinopulmonary disease, chronic non-infectious diarrhea, and opportunistic infections. The prognosis in patients with Good's syndrome appears to be worse than in those with X-linked

agammaglobulinemia (XLA) and common variable immune deficiency (CVID) [2]. In a case series of 240 patients, the 5-year survival rate was almost 100% for patients with XLA and CVID, compared to 70% for patients with Good's syndrome. The 10-year survival rate dropped to 33% in Good's syndrome patients, compared to 95% for patients with XLA and CVID [3]. Morbidity and mortality in Good's syndrome is attributable to secondary processes such as infections, autoimmunity and hematological dysfunction, rather than the thymoma itself.

There have only been three cases of Good's syndrome associated with mycobacterium, and only one case with a cavitary lesion in the lungs [4, 5]. We present here a unique case of Good's syndrome with a non-mycobacterial cavitary lesion.

CASE PRESENTATION

A 56-year-old Ethiopian male immigrant was admitted with persistent fever and chills, cough, night sweats, and weight loss. He had a past medical history significant for a type A thymoma that was resected 3 years prior to admission. An outpatient pulmonologist who had seen him for suspected tuberculosis referred him to the Inpatient Medicine Unit following a computed tomography (CT) scan of the chest that revealed a 3.5 cm right hilar region mass. There were also two additional smaller adjacent nodules in the right lower lobes, and scattered areas of tree and bud nodularity.

The patient was subsequently admitted to Ronald Reagan UCLA Medical Center and placed on respiratory isolation. Here, he reported a history of fatigue and dyspnea on exertion, as well as recurrent sinopulmonary infections that intermittently responded to antibiotics. These infections often recurred in the setting of irritable bowel syndrome D (IBS-D) symptoms, hallmarked by diarrhea.

At the time of admission, he had a low-grade fever with otherwise normal vital signs and oxygen saturation on room air. Blood tests were significant for an absolute lymphocyte count of 1,000 cells/μL, and hemoglobin of 11.7 g/dL. The only other abnormalities were decreases in albumin and protein levels.

A chest CT scan on admission revealed an irregular, cavitating soft-tissue right hilar mass involving the posterior segment of the right upper lobe and superior segment of the right lower lobe. In addition, there were focal areas of mucous impaction and bronchiectasis with multiple diffuse scattered clusters of bronchocentric micronodules, many in a tree-in-bud nodularity (Fig. 1).

Cultures of blood, sputum and urine were negative for an extensive workup that included human immunodeficiency virus (HIV), cytomegalovirus (CMV), acid-fast bacillus, *Histoplasma*, *Aspergillus* and coccidioidomycosis. Finally, a biopsy of the cavitary lesion of the lung showed ulceration with acute and chronic inflammation. Cultures from a transbronchial biopsy were negative. Grocott's methenamine silver (GMS) staining was negative for fungal organisms, and there was no evidence of malignancy.

On the second day of hospitalization, induced sputum was positive for *Pneumocystis jiroveci* and *Moraxella catarrhalis*. Given the history of recurrent pneumonia, lymphopenia and an opportunistic infection in the setting of a HIV negative patient, a more thorough immunologic workup was performed. As shown in Table 1, low levels of CD3 (540/cmm) and CD4 (250/cmm) T cells were found, while CD8 (264/cmm), and CD16&56 (93/

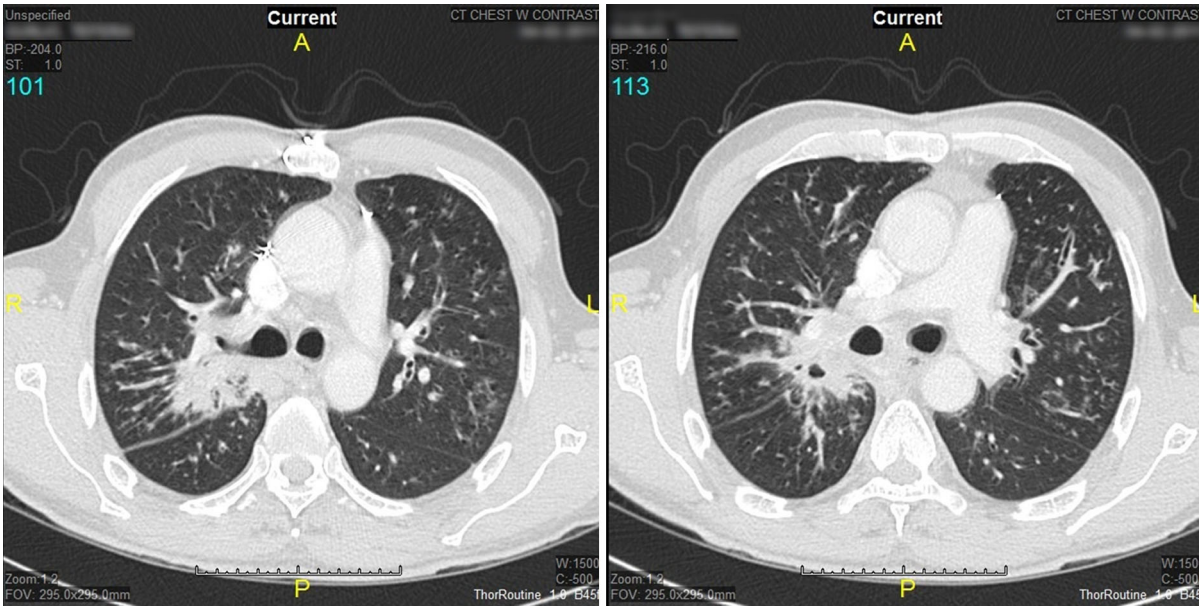

Fig. 1 Computed tomography (CT) scan of the chest with a right hilar region mass, mucous impaction and bronchiectasis

Table 1 Lymphocyte and immunoglobulin enumeration

T/B/NK cell subsets	Absolute count (normal range)	Percentage (normal range)
CD3	540/cmm (841–2,402)	86% (59–86)
CD4	250/cmm (355–1,426)	42% (29–62)
CD8	264/cmm (255–1,090)	45% (16–41)
CD19	1/cmm (10–590)	<1% (7–25)
CD16&56 (NK cells)	93/cmm (71–477)	15% (4–19)

Immunoglobulins	Level (normal range)
IgA	20 mg/dL (80–400)
IgG	176 mg/dL (690–1,660)
IgM	<5 mg/dL (37–318)

CD cluster of differentiation, *Ig* immunoglobulin, *NK* natural killer

cmm) were normal. The B cell lineage was profoundly deficient, starting with CD19 (1/cmm), and carried through with immunoglobulin M (IgM) (<5 mg/dL), IgA (20 mg/dL), and IgG (176 mg/dL); he showed no antibody response to any of the 14 pneumococcal serotypes examined. Furthermore, a lymphocyte proliferation assay demonstrated a significantly decreased response to tetanus and candida, as compared to a normal control.

The patient was subsequently treated for pneumonia with sulfamethoxazole/trimethoprim double strength for 3 weeks followed by sulfamethoxazole/trimethoprim single strength for prophylaxis. He was also started on monthly intravenous immunoglobulin (IVIG) replacement, which was continued after discharge. Over 6 months following discharge the patient remains free of hospitalization, reporting a reversal of his dyspnea, and a drastic improvement in his quality of life. He continues to be monitored for anemia, as there have been reported cases of Good's syndrome with pure red cell aplasia [6, 7].

Informed consent was obtained from the patient for being included in the study.

DISCUSSION

The 2005 practice parameters define Good's syndrome as a subset of CVID [8]; however, the reduced number of peripheral B cells seen in Good's syndrome is not a feature of CVID, where only impairment in B cell maturation is usually observed. Diagnosis remains based on clinical criteria. However, genetic analysis has begun to elucidate the etiology of Good's syndrome, which, like CVID, appears to affect proteins involved in the proliferation and differentiation of B cells [9, 10]. In a systematic review of 152 patients with Good's syndrome, 42% of patients were diagnosed with thymoma prior to being diagnosed with hypogammaglobulinemia, infection or diarrhea, while in 38% of patients the diagnoses were made almost simultaneously—i.e., within 2 months of each other [2]. Since 10% of patients diagnosed with a thymoma continue to develop hypogammaglobulinemia, an immunologic workup at regular intervals can be very helpful in preventing opportunistic infections. Additionally, patients with hypogammaglobulinemia should be screened for thymoma, as 10% will continue to present with a thymoma [2]. Good's syndrome shares many features with CVID, but unlike the latter and the more serious XLA, it carries a much worse prognosis. Aside from the additional involvement of thymic dysfunction, one of the reasons for inferior outcomes is the greater delay in diagnosis [11].

In contrast to other humoral immune defects, patients with this syndrome can develop opportunistic infections, and the prognosis appears less favorable compared with XLA or CVID [3]. Immunological workup, including T cell subsets, B cells and quantitative immunoglobulins, should be considered as part of the routine diagnostic evaluation in patients with a thymoma and recurrent infections.

It is important to note that Good's syndrome may progress even after thymectomy and corticosteroid treatment [12, 13]. However, early recognition and treatment with antibiotics or immunoglobulin replacement can change the natural course of this rare condition, and prove to be successful in keeping the patient symptom free [14].

ACKNOWLEDGMENTS

This work was not supported financially or otherwise. All named authors meet the ICMJE criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

Conflict of interest. Dr. Tachdjian, Dr. Keller and Dr. Pfeffer declare no conflict of interest.

Compliance with ethics guidelines. Informed consent was obtained from the patient for being included in the study.

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