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Case report

Good's syndrome with clinical manifestation after thymectomy: A case report

Ryutaro Furukawa[a,*], Masahiro Yanagiya[b], Jun Matsumoto[b], Hirotsugu Hashimoto[c], Hajime Horiuchi[c], Kazuhiro Usui[a]

[a] Division of Respirology, NTT Medical Center Tokyo, 5-9-22 Higashigotanda, Shinagawa-ku, Tokyo, Japan
[b] Department of General Thoracic Surgery, NTT Medical Center Tokyo, 5-9-22 Higashigotanda, Shinagawa-ku, Tokyo, Japan
[c] Department of Diagnostic Pathology, NTT Medical Center Tokyo, 5-9-22 Higashigotanda, Shinagawa-ku, Tokyo, Japan

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ABSTRACT

Good's syndrome is a rare condition of immunodeficiency that is characterized by thymoma and hypogammaglobulinemia. A 74-year-old Japanese woman underwent total thymothymectomy for type AB thymoma (2015 WHO classification). She developed recurrent infectious diseases caused by *Escherichia coli* (bacteremia), *Streptococcus pneumoniae* (pneumonia and bacteremia) and *Pseudomonas aeruginosa* (bacteremia) in the year after thymectomy. The serum levels of immunoglobulin were significantly low (IgG 157mg/dL), which suggested that her infectious diseases were associated with Good's syndrome. Although she began receiving intravenous immunoglobulin every four weeks, she died of pneumonia a week after the second administration of immunoglobulin. When physicians encounter patients with recurrent infection who have a medical history of thymoma, the detection of hypogammaglubulinemia can be a key clue to the diagnosis of Good's syndrome.

1. Introduction

Good's syndrome is a rare condition of immunodeficiency that is characterized by thymoma and hypogammaglobulinemia; the condition was first reported by Good in 1954 [1]. The clinical symptoms include recurrent respiratory infection and diarrhea. The prognosis of Good's syndrome is reported to be poor, and the effectiveness of thymectomy in controlling Good's syndrome is controversial. We herein report a case of Good's syndrome that was associated with oral lichen planus, repeated pneumonia and bacteremia, which developed after thymectomy for thymoma.

2. Case report

A 74-year-old Japanese woman with a mediastinal tumor was referred to our hospital (Fig. 1A). She had been regularly visiting a dentist for over five years due to oral pain caused by oral lichen planus, which had been diagnosed by biopsy. She underwent total thymothymectomy and the tumor was pathologically diagnosed as type AB thymoma (the 2015 World Health Organization Classification of tumors of the thymus [2]) (Fig. 1B and C). She had no symptoms consistent with myasthenia gravis. Antibodies to acetylcholine receptor were not detectable.

Ten months after thymectomy, she was admitted to our hospital because of fever. Two blood culture sets were positive for *Escherichia coli*. A urine culture was negative, and other routes of infection were unclear. She was treated with intravenous ceftriaxone for two weeks.

Nine months later, she was admitted again for a one-month history of cough and a five-day history of fever. An oral examination showed several mucosal white lesions which had been formerly diagnosed as lichen planus. Chest X-ray and CT showed the infiltration of the right lung. Blood and sputum cultures were positive for *Streptococcus pneumoniae*, which led to a diagnosis of pneumococcal pneumonia accompanied by invasive pneumococcal disease (IPD). She recovered after treatment with intravenous ceftriaxone for two days and ampicillin for six days and was able to leave hospital. Oral amoxicillin was prescribed for one week after she was discharged.

At four days after the cessation of amoxicillin, she developed cough and fever, and was again admitted to our hospital. Chest radiography showed bilateral pneumonia. A blood culture was positive for both *S. pneumoniae* and *Pseudomonas aeruginosa*.

We investigated the cause of her repeated infectious diseases. She had no history of primary immunodeficiency. The patient was negative for antibodies to human immunodeficiency virus and human T-cell leukemia virus type 1. The serum immunoglobulin levels were measured, revealing significant hypogammaglobulinemia (IgG 157mg/dL, IgA 20mg/dL, IgM < 10mg/dL). Her repeated and frequent infections

* Corresponding author.
E-mail address: rfurukawa-tky@umin.ac.jp (R. Furukawa).

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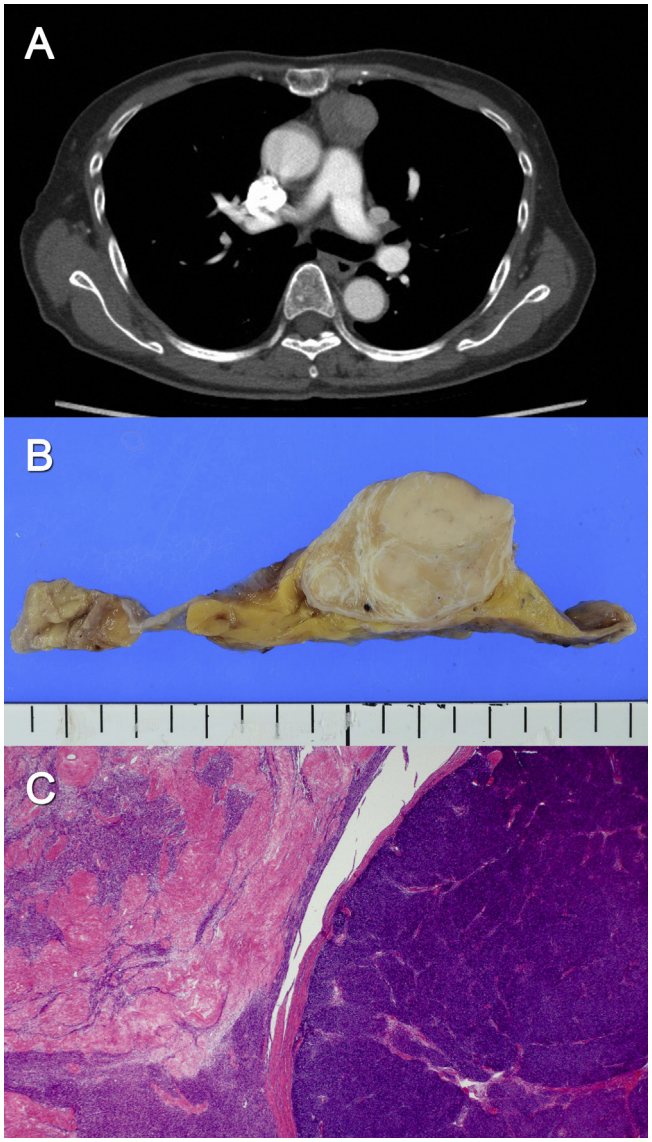

Fig. 1. Chest computed tomography revealed a well-margined mass in the anterior mediastinum with a diameter of 31 mm (A). Total thymothymectomy was performed (B), and the histological findings of the mediastinal tumor confirmed the diagnosis of type AB thymoma (2015 WHO classification). Some areas had storiform pattern of spindle shaped epithelial cells and others had increased numbers lymphocytes with round or polygonal epithelial cells (C).

were associated with hypogammaglobulinemia-related immunodeficiency. Considering her medical history of thymoma resection, her conditions were consistent with Good's syndrome.

Pneumonia and bacteremia were successfully treated with intravenous ceftriaxone for one week followed by meropenem treatment for two weeks. Although she began receiving intravenous immunoglobulin (15g/body; 375mg/kg) every four weeks, she developed pneumonia again and died one week after the second administration of immunoglobulin.

3. Discussion

We experienced a case of Good's syndrome in a patient who repeatedly suffered from infectious diseases after thymectomy for thymoma. To the best of our knowledge, this is the first case of Good's syndrome that developed in association with IPD. Her immunological condition deteriorated after thymectomy, and she died of repeated pneumonia despite the regular administration of intravenous immunoglobulin.

Good's syndrome is a relatively rare condition of immunodeficiency that develops in patients with thymoma. Thymoma is often associated with variable immunological abnormalities. Bernard et al. reported that 47 patients of 85 patients with thymoma had autoimmune disease [3]. Myasthenia gravis was the most common autoimmune disease (n = 33); one patient was diagnosed with Good's syndrome. In other studies, the reported incidence of hypogammaglobulinemia was 6–11% [4].

In our case, it took 19 months after thymectomy to make diagnosis of Good's syndrome. A systemic review of 152 cases of Good's syndrome in the literature showed that the diagnosis of thymoma preceded the diagnosis of hypogammagobulinemia, infection, or diarrhea by 3 months–18 years in 42% of the patients [5]; this suggested that hypogammagobulinemia is difficult to recognize during the clinical course of thymoma. Good's syndrome is under-recognized in patients with thymoma.

The patient in this report had been suffering from oral pain due to lichen planus for more than five years before the diagnosis of thymoma. Lichen planus is a T-cell mediated chronic inflammatory disease of the skin and mucous membranes. Oral lesions are reported to be common in patients with thymoma [5]; thus oral examinations are important when treating patients with thymoma.

Our case developed bacteremia caused by *E. coli, S. pneumoniae* and *P. aeruginosa*. Bacteremia and recurrent sinopulmonary infection are common forms of infectious disease [5]; encapsulated bacteria, such as *Haemophilus influenzae*, *Pseudomonas* species, and *S. pneumoniae* were the most common pathogens reported [5]. *S. pneumoniae* is a common pathogen of pneumonia; however, to our best knowledge, there have been no previous reports of IPD associated with Good's syndrome.

Although immunoglobulin replacement therapy has been reported to improve infection control in patients with Good's syndrome, our patient died of pneumonia after receiving a standard dose of intravenous immunoglobulin (300–500 mg/kg every three to four weeks) [6]. The prognosis of Good's syndrome is reported to be poor in comparison to patients with other conditions of immunodeficiency. One study reported that 33% of patients with Good's syndrome were alive at 10 years after the diagnosis; in contrast 95% of patients with common variable types of immunodeficiency were alive at 10 years after the diagnosis [7]. Thymectomy, which is recommended for patients with other autoimmune diseases, such as myasthenia gravis, does not improve the immunological condition of patients with Good's syndrome [5].

The relationship between thymoma and immunodeficiency has been incompletely understood, and no clear diagnostic criteria for Good's syndrome have been established. The principal feature of Good's syndrome is humoral immunodeficiency caused by hypogammaglobulinemia; however, cell-mediated immunity is also impaired. Cytokines from bone marrow stromal cells may inhibit the growth and differentiation of thymic and B cell precursors [8]. Another hypothesis is that T cells from thymoma may impair the growth of B cells and immunoglobulin production [8].

In summary, we reported a case of Good's syndrome in a patient who experienced repeated infection, including IPD. The diagnosis of oral lichen planus and frequent infection helped us to diagnose her condition as Good's syndrome. Therefore, when treating patients with recurrent infection and autoimmune diseases who have a medical history of thymoma, the recognition of hypogammaglubulinemia can be a key clue to making an accurate clinical diagnosis.

Conflicts of interest

None of the authors have any conflicts of interest to declare.

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