Tuberculous lymphadenitis in a patient with Good syndrome

Introduction

Good syndrome, thymoma complicated with hypogammaglobulinaemia, is a rare disease that causes combined B and T cell immunodeficiency in adults. This immunodeficiency renders patients with Good syndrome very susceptible to recurrent infections of encapsulated bacteria, fungi and viruses. This article describes a rare case of a patient with Good syndrome who presented with tuberculous lymphadenitis and *Pseudomonas aeruginosa* pneumonia.

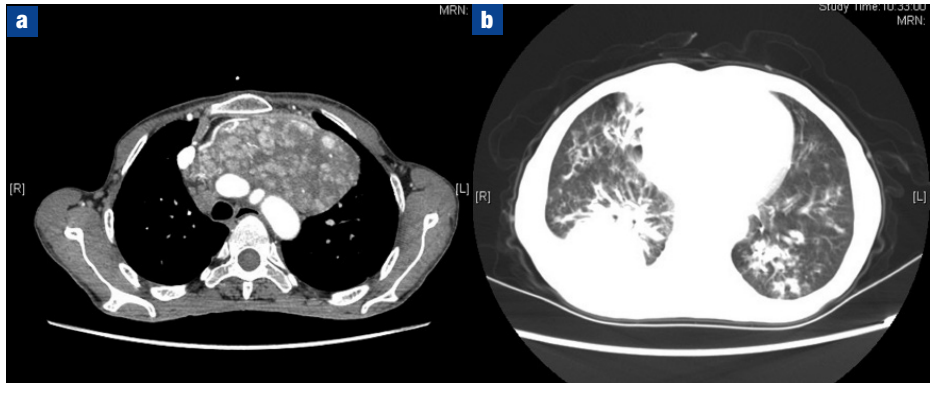
Discussion

The correlation of thymoma and adult-onset hypogammaglobulinaemia was first described by Dr RA Good in 1954 (Good, 1954). The incidence of thymoma was reported as 10% in patients with adult-onset hypogammaglobulinaemia (Engels and Pfeiffer, 2003), while hypogammaglobulinaemia was found in up to 6–11% of patients with thymoma (Rosenow and Hurley, 1984). Immunodeficiency with thymoma, a broader classification, was defined as Good syndrome (Kelesidis and Yang, 2010).

The primary manifestations of Good syndrome appear late in life, usually between 40 and 70 years old (Miyakis et al, 2006). No gender differences are observed. Good syndrome has a worldwide distribution with approximately half of the cases (47%) in Europe but is rarely seen in China. The common histological types of thymoma in Good syndrome include AB (41.7%), B2 (25%), B1 (12.5%), and carcinoma (8.3%) (Kelesidis and Yang, 2010). In this case, the thymoma was the AB variant.

The immunodeficiency of Good syndrome is characterized by absence or low counts of circulating B lymphocytes, marked decrease in all classes of immunoglobulins, an abnormal CD4+:CD8+ T lymphocyte ratio, and CD4+ T cell lymphopenia. The absence of circulating B cells, profound hypogammaglobulinaemia and CD4 lymphopenia in this case confirmed the diagnosis of Good syndrome, but CD4 lymphopenia also can be found in the context of active tuberculosis and *Pseudomonas* pneumonia. Therefore, the absence of circulating B cells and profound hypogammaglobulinaemia provided stronger evidence for the diagnosis. Functional abnormality of white blood cells, leukopenia and neutropenia are considered related to immunodeficiency in Good syndrome.

Figure 1. Chest computed tomography scan. **a.** A large well-circumscribed mass (measured 5.7×11.5 cm) in the anterior mediastinum. **b.** Bronchiectasis with patchy lesions over both lower lungs.



CASE REPORT

A 52-year-old Chinese woman with a 4-month history of multiple neck masses, persistent productive cough and intermittent fever was admitted to the authors' hospital. She had suffered recurrent lower respiratory tract infection presenting with large amounts of yellow sputum for 6 years.

Physical examination demonstrated multiple neck masses (maximum measured 1.7×2.5 cm), and moist rales over both lung bases. Blood chemistry revealed a decrease in serum levels of all immunoglobulins including IgG = 178 mg/dl, IgA = 423 mg/dl and IgM <4 mg/dl. The CD4+ T-cell count was reduced to 240/ul and the CD4+:CD8+ ratio was 0.24. Flow cytometry showed CD4+ lymphocyte 16.9%, CD8+ lymphocyte 70.3%, but no evidence of either mature or immature B cells. Human immunodeficiency virus antibodies and polymerase chain reaction were negative, and no protein was found in the urine.

A chest computed tomography scan revealed a large well-circumscribed mass (measured 5.7×11.5 cm) in the anterior mediastinum (*Figure 1a*) and bronchiectasis with patchy lesions over both lower lungs (*Figure 1b*). The mass in the anterior mediastinum was identified as a type AB thymoma by ultrasound-guided percutaneous puncture biopsy (*Figure 2*). The presence of *Mycobacterium tuberculosis* was confirmed by right neck lymph node biopsy (*Figure 3*), and *Pseudomonas aeruginosa* pneumonia by positive sputum and blood cultures, leading to a diagnosis of Good syndrome.

Thymectomy, intravenous immunoglobulin replacement treatment and antibiotics were suggested but were refused for financial reasons. The patient died of pneumonia 1 month later.

Dr Li Luo Is Associate Chief Physician in the Institute of Respiratory Medicine, Xinqiao Hospital, Chongqing, P.R. China

Dr Wen Zhang is Resident Physician in the Institute of Respiratory Medicine, Xinqiao Hospital, Chongqing, P.R. China

Dr Chuan-wei Li is Attending Physician in the Department of Cardiology, Daping Hospital, Chongqing, P.R. China

Dr Xue-feng Tang is Associate Chief Physician in the Department of Pathology, Xinqiao Hospital, Chongqing, P.R. China

Correspondence to: Dr W Zhang (zhangwen1564@foxmail.com)

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Figure 2. The histopathological findings of the mass in the anterior mediastinum obtained by ultrasound-guided percutaneous puncture biopsy. Spindle cell mixed with small lymphoid cell. Haematoxylin and eosin staining, ×100.

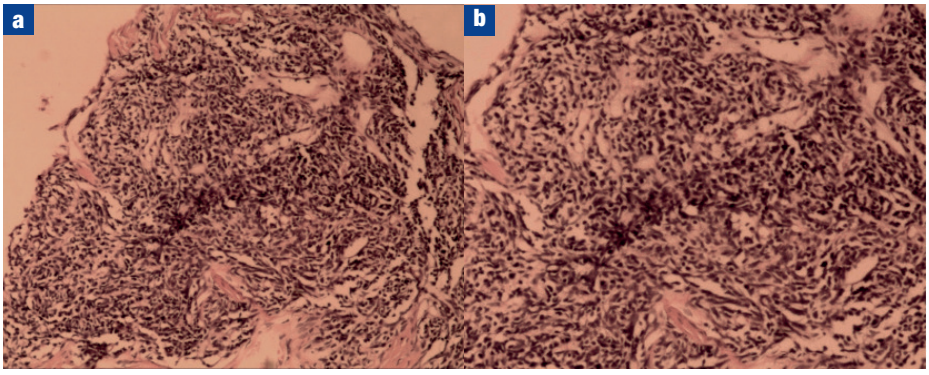
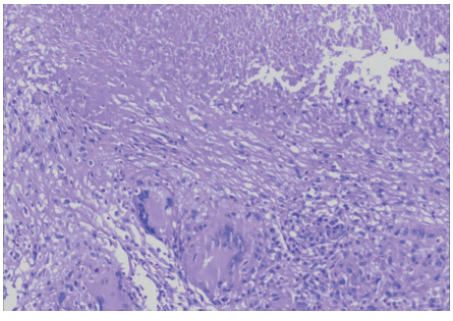


Figure 3. The histopathological findings of right neck lymph node tissue – polynuclear granulomatosis and caseous necrosis. Haematoxylin and eosin staining, ×100.



As a result of both humoral and cell-mediated immune deficiency, patients with Good syndrome have increased susceptibility to bacterial, fungal and viral infections (Khanna et al, 2004; Koriyama et al, 2004; Agarwal and Cunningham-Rundles, 2007). Recurrent infections were reported in almost 85% of patients with Good syndrome. The mortality in patients with Good syndrome was 44.5%, of which 59.6% of patients died as a result of infection (Kelesidis and Yang, 2010). Furthermore, the upper and lower respiratory tract is the most susceptible site of recurrent infections. The most frequent identified pathogens are encapsulated bacteria. As already reported (Kelesidis and Yang, 2010) the pathogens of recurrent sinopulmonary infection were *Haemophilus influenzae* (24.5%), *Pseudomonas* spp. (22.6%), *Klebsiella* spp. (13.2%), *Streptococcus pneumoniae* (13.2%) and *Staphylococcus aureus* (7.5%). In this case, *P. aeruginosa* pneumonia was consistent with the common infections.

Opportunistic infections, which are usually observed in severe cell-mediated immunodeficiency diseases, are a distinctive feature of Good syndrome, in particular cytomegalovirus and *Candida* infections. Compared to other disorders of cell-mediated immunity, the incidence of *Mycobacterium tuberculosis* infection in patients with Good syndrome is very low. Tuberculous lymphadenitis was confirmed by right neck lymph node biopsy in this case. The characteristics of reported *M. tuberculosis* infection in patients with Good syndrome are summarized in *Table 1* (available at www.bjhm.co.uk). However, the reasons for the rare incidence of *M. tuberculosis* in patients with Good syndrome are still unknown. Significantly underdiagnosed Good syndrome in areas of high tuberculosis endemicity, especially in China, may be the cause of the rarity of previous cases.

Thymoma was diagnosed after the recorded infection in 20% of patients with Good syndrome, and in 38% of patients the diagnoses were made within 2 months of each other (Kelesidis and Yang, 2010). This patient suffered recurrent lower respiratory tract infection for 6 years with a diagnosis of bronchiectasis. Good syndrome was not diagnosed until hypogammaglobulinaemia and thymoma were found. When recurrent infections are encountered, immunocompromised status should be considered. A chest computed tomography scan and immunological examinations are needed to search for Good syndrome (Zabsonré et al, 2012). Moreover, Good syndrome should be considered when adults with a history of thymoma, especially AB type, suffer from recurrent infections. Thymectomy is recommended in patients with Good syndrome for its favourable effect on autoimmune disorders, but recurrent infections still exist after thymectomy. It indicates thymectomy cannot improve the immunodeficiency state completely (Wang et al, 2015). BJHM

LEARNING POINTS

- The incidence of *Mycobacterium tuberculosis* infection in patients with Good syndrome is very low.
- Clinicians should search for evidence of immunological dysfunction in thymoma patients presenting with recurrent infections.
- Increased knowledge of the clinical and immunological profile of Good syndrome may increase its early recognition and improve the prognosis.

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Table 1. Characteristics of Good syndrome patients with tuberculosis infection

Characteristics		Case 1	Case 2	Case 3	Case 4	Current case
Year, centre		1966, Veterans Administration Hospital, USA	1985, University of Turku, Finland	2009, Tri-Service General Hospital, Republic of China	2012, Donostia University Hospital, Philippine Islands	2015, Xin Qiao Hospital of The Third Military Medical University, Republic of China
Sex, age of Good syndrome diagnosis (years)		M, 74	M, 58	M, 28	M, 76	F, 52
Family history of immunodeficiency		No	Not known	Not known	No	No
Presenting feature		Recurrent infections	Recurrent infections	Recurrent infections	Mediastinal mass (thymoma)	Recurrent infections
Thymoma histology		Type AB	Type B1	Not known	Type A	Type AB
Age at tuberculosis diagnosis (years)		73	59	28	70	52
Site of tuberculosis		Bilateral, apical lungs	Left ear and lungs	Bilateral lungs, pharyngeal, head and neck lymph nodes	Not known	Neck lymph node
Immunological hypogammaglobulinaemia		Yes	Not known	Not known	Yes	Yes
IgG		Low	Normal	Not known	Low	Low
IgA		Low	Low	Not known	Low	Low
IgM		Low	Low	Not known	Low	Low
Absent B cells		Not known	Yes	Yes	Yes	Yes
Reduced CD4+:CD8+ T-cell ratio		Not known	Yes	Yes	Yes	Yes
Reduced CD4+ T-cell count		Not known	Not known	Yes	Yes	Yes
Infections	Pulmonary (pneumonia)	Yes	Yes	Yes	Yes	Yes
	Chronic diarrhoea	Yes	No	No	No	No
	Others	Urinary tract	No	No	Tetanus	No
Infections caused by	*Streptococcus pneumoniae*	Yes	No	No	Yes	No
	Haemophilus influenzae	Yes	No	No	Yes	No
	Pseudomonas aeruginosa	No	No	No	Yes	Yes
	Cytomegalovirus	No	No	No	No	No
	Candida	No	No	No	No	No
	Others	*Aerobacter aerogenes*, *Salmonella worthington*	No	*Pneumocystis jirovecii*, *Toxoplasma gondii*	*Enterobacter asburiae*	No
Autoimmune disease associated		No	Myasthenia gravis	No	No	No
Treatment	Intravenous immunoglobulin	Yes	Yes	No	Yes	No
	Anti-tuberculosis	Yes	Yes	Yes	Not known	Yes
Thymectomy		Yes	Yes	Yes	Not known	No