Case Report

A Case of Good's Syndrome Presenting with Pulmonary Tuberculosis

Arunabha Datta Chaudhuri[1], Sumit Roy Tapadar[1], Aparup Dhua[2], Palash Nandan Dhara[1], Saumen Nandi[3] and Sabyasachi Choudhury[4]

Department of Pulmonary Medicine, R.G. Kar Medical College[1], Department of Pulmonary Medicine, Midnapore Medical College[2], Malda Medical College, Malda[3] and Medical College[4], Kolkata, India

Abstract

Adult onset immunodeficiency associated with thymoma is a rare condition. The combination of hypogammaglobulinemia, reduced number of peripheral B and CD4+ T cells, along with thymoma constitutes Good's syndrome (GS). This immunodeficiency condition is often complicated with opportunistic infection with organisms, like bacteria (*Haemophilus influenzae, Streptococcus pneumonia* etc), viruses (*Cytomegalovirus, Herpes simplex* etc), fungi and protozoa. We present an unusual case of Good's syndrome with pulmonary tuberculosis (PTB). A 40-year-old man presented with sputum-positive PTB and was started on anti-tuberculosis treatment. Subsequently, he developed symptoms and findings consistent with thymoma and other components of Good's syndrome. Although patients of Good's syndrome are susceptible to various opportunistic infections, infection with *Mycobacterium tuberculosis* is uncommon. Evidence of recurrent infections or some opportunistic infection in a thymoma patient should trigger a suspicion of Good's syndrome.

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Key words: Thymoma, Good's syndrome, Tuberculosis, Opportunistic infection.

Introduction

Good syndrome is a rare, adult onset, combined B- and T- cell immunodeficiency with thymomas, first described by Dr Robert Good in 19541. Its main components are: thymoma, hypogammaglobulinemia, low or absent B cells, deficient CD4+Tcell and an abnormal CD4: CD8 ratio in peripheral blood.[2,3]

The average age group commonly affected by Good's syndrome is 40 to 70 years. The expert committee of the World Health Organization and International Union of Immunological Societies on primary immunodeficiency has classified Good's syndrome as a distinct clinical entity.[4] The pathogenesis, aetiology of Good's syndrome is still unknown. However some evidence indicates some defect in the bone marrow itself, e.g. pre-B cell arrest, impaired maturation of cell subsets.[5]

Case Report

A 40-year-old male, smoker, with a history of repeated sino-pulmonary infections since the past few years, was diagnosed to be having sputum-positive pulmonary tuberculosis (PTB). His chest radiograph showed patchy lesions throughout the right lung field (Figure 1). He was started on treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol. He responded well and sputum conversion was achieved at the end of two months of treatment. But, he returned back with a new set of symptoms while on the continuation phase of tuberculosis treatment. This time

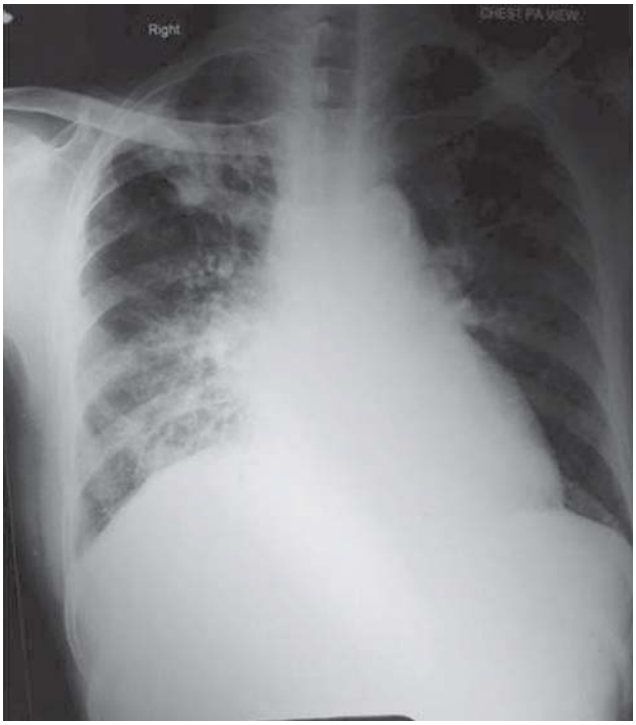

Figure 1. Chest radiograph (postero-anterior view) showing patchy lesions throughout the right lung field.

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Correspondence and reprint requests: Dr Arunabha Datta Chaudhuri, BF-130, Sector – I, Salt Lake City, Kolkata-700 064 (West Bengal), India; E-mail: arunabhadc@rediffmail.com

there was shortness of breath, dull aching central chest pain and hoarseness of voice, which compelled him to return.

On clinical examination, the only positive findings were, dullness on percussion over the manubrium sterniand reverse D'Espine sign on auscultation (i.e., bronchial breath sound and bronchophony heard over supracardiac vessels area). A repeat chest radiograph revealed widening of mediastinal shadow involving the right para-tracheal–parahilar and left parahilar areas and partial resolution of previous tubercular lesions in the right lung field (Figure 2). Fibreoptic laryngoscopy showed left vocal cord palsy. Contrast-enhanced computed tomography (CECT) of thorax

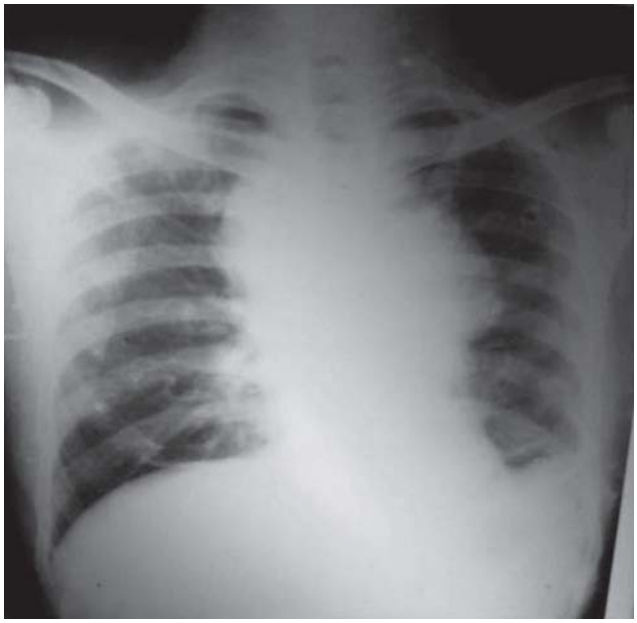

Figure 2. Chest radiograph repeated after 3 months, showing widening of mediastinal shadow involving the right paratracheal-parahilar and left parahilar areas and partial resolution of previous tubercular lesions in the right lung field.

revealed a large anterior mediastinal mass, having heterogeneous texture and irregular outline without significant contrast enhancement or involvement of neighbouring structures (Figure 3). A core-needle biopsy under CT guidance was performed. Histopathology showed angulated lobules separated by fibrous band. Lobules contained sheets of small cells having round nuclei with dense chromatin and scanty cytoplasm, resembling lymphoid cells along with scattered thymic epithelial cells with round to oval nuclei and pale staining cytoplasm and a few Hassall corpuscles (Figure 4). On immunohistochemistry, the thymic epithelial cells were positive for cytokeratin and the background lymphoid cells had a naïve T-cell phenotype (TdT+; CD3+; CD20+). This was consistent with thymoma. Further investigations at this juncture, revealed that the patient had: (1) hypogammaglobulinemia: IgA = 22 mg / dL (Reference

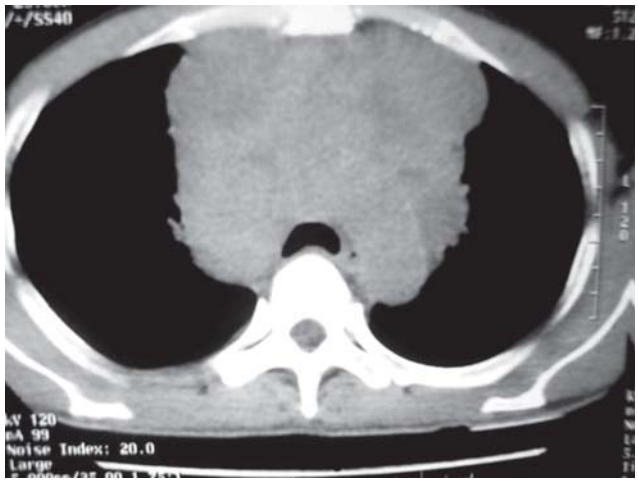

Figure 3. Contrast-enhanced CT scan of thorax showing a large anterior mediastinal mass lesion.

range = 56 – 352 mg / dL), IgM = 48 mg / dL (Reference range = 70 – 312 mg / dL), IgG = 316 mg / dL (Reference range = 639 – 1329 mg / dL); (2) reduced number of CD 4+ T cells = 348 / mL (Reference range = 588 – 1202 mg / dL); and (3) B-cell depletion (only 1% of total lymphocytes).

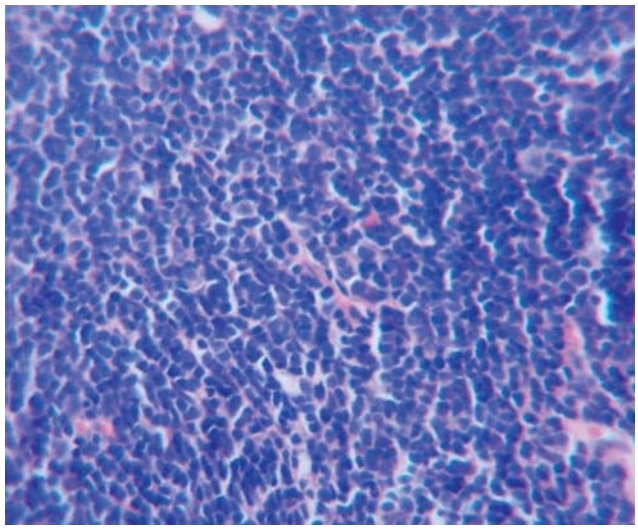

Figure 4. Microphotograph showing histopathology of the thymic mass (Haematoxylin and Eosin, × 400).

Anti-tuberculosis treatment was continued and the tumour was surgically removed via a median sternotomy. There was no per-operative or histopathological evidence of involvement of neighboring structures by the thymoma. The patient is now doing well and he is asymptomatic. He was advised intravenous immunoglobulin (IVIG), but he could not afford it.

Discussion

Good's syndrome, an adult onset combined immunodeficiency with thymomas, is a rare entity. Western literature reports the incidence of Good's

syndrome as 5% to 10% of all thymomas, whereas it is rare in the eastern part of the globe, 0.2% – 0.3% as per Japanese literature.[1] Tarr and colleagues[2] has reviewed 51 cases of Good's syndrome. Among them capsulated organisms like *Haemophilus influenza* were found in 24% cases (most common), followed by *Streptococcus pneumonia* in 8% cases and other gram-negative organisms lie *Pseudomonas spp*, *Klebsiella spp* etc. Among other infections, mucocutaneous candidiasis was found in 24% cases, and in patients having chronic diarrhoea, protozoa like *Giardia lamblia* and enteropathic organisms like *Salmonella spp* and *Campylobactorjejuni* were reported.[2] In a report from the USA,[3] concomitant infection with *Clostridium difficile* and *Babesiamicroti* and colonisation of lower respiratory tract with *Pseudomonas aeruginosa* causing repeated lower respiratory tract infection and evidence of Kaposi's sarcoma on feet were described.

Unlike other humoral immune defects, like common variable immunodeficiency and X-linked agammaglobulinemia, opportunistic infection with *Cytomegalovirus* and *Pnuemocytis carini* are common in Good's syndrome, as observed by Kelleher and Misbah.[4] Another interesting fact is that, in comparison to human immunodeficiency virus-infected patients, opportunistic infections can occur at a higher level of CD4+ T cell count in Good's syndrome.[2] Opportunistic infection by *Mycobacterium tuberculosis* has been uncommonly described in Good's syndrome, in contrast to HIV-infected patients. Tarr *et al*[7] found only two cases of tuberculosis among 51 cases of Good's syndrome.

Good's syndrome is commonly diagnosed in 4th or 5th decade, and the mean age of symptomatic presentation is 56 years (range 29–75 years). The mean age for the detection of thymomas and hypo-gammaglobulinemia is 62 years (range 41–79 years).[2] In our case, the patient was 40 years old. Good's syndrome occurs with the same frequency in men and women. Presenting symptoms may be variable. Some may be asymptomatic, having an anterior mediastinal mass as incidental finding on chest radiograph; while others may have compressive symptoms like hoarseness, cough, dysphagia, chest pain, and dyspnoea.[5] In our case, symptoms like hoarseness and dyspnoea compelled the patient to re-visit and eventually the intra-thoracic mass was found. The immunodeficiency may occur in an already diagnosed case of thymoma[2,6] or may antedate the symptomatic manifestation of thymoma,[2] as in our case. Our patient already had a history of recurrent sino-pulmonary infections and sputum-positive PTB, for which he had received more than two months treatment before symptoms of thymomas appeared.

For the diagnosis of Good's syndrome, chest radiograph (posterio-anterior view) usually detects 80% of thymomas as anterior mediastinal mass.[7] On the other hand it may be missed or remain inapparent. One study reported a miss-rate of 25% thymoma masses, causing a diagnostic delay of 41 months.[7] Thus, it proves the need for computed tomography (CT) scan of thorax if a clinical suspicion of thymomas exists which can also give anatomical details of extent of thymomas and can stage it as well.[8,9] Flow cytometry, especially the single platform flow cytometry technology gives the most reproducible result in innumeration of the B- and T- cell subsets.[10] Histopathology of thymomas in Good's syndrome is usually benign, commonly spindle cell variant. Thymic carcinomas are uncommon.[11]

Treatment of thymomas is surgical — either removal or debulking.[9] Removal does not reverse the immunological defects. Immunoglobulin replacement therapy is required for antibody deficiency.[4] The most strategic prognostic indicator is totality of tumour removal.[9,12]

In conclusion, our case of Good's syndrome with *Mycobacterium tuberculosis* infection, which antedates the clinical manifestation of thymoma, gives us the following insights — Serum immunoglobulin level and amount of B- cell and T- cell subsets should be measured in all patients of thymomas; CT scan of thorax should be considered, if clinical suspicion of thymomas exists; *Mycobacterium tuberculosis* may be associated with Good's syndrome; and If a case of tuberculosis re-visits with microbiological improvement but clinical deterioration, one should investigate thoroughly for other underlying disorders.

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