

Good Syndrome, a rare disease that physicians cannot afford to overlook; Case report and review of literature

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Introduction

Good syndrome (thymoma with immunodeficiency) is a rare cause of immunodeficiency.¹ There is a combined B and T cell immunodeficiency with hypogammaglobulinemia, reversal of the CD4/CD8 ratio and reduced or absent B cells causing an increased susceptibility to bacterial, viral and fungal infections. It is classified as a primary immunodeficiency,² and patients usually present with recurrent infections or a mediastinal mass.³ The infrequency with which it is encountered makes Good syndrome a diagnostic challenge.

Keywords: Good syndrome, Aspergillus.

Case Report

A 60 years old male with no co-morbidities presented with complaints of chest pain to an outside hospital. Initial investigations revealed an anterior mediastinal mass, which was excised with biopsy confirming the diagnosis of thymoma. The patient then presented to our hospital in May 2011. Since the pathology report documented positive tumour margins, the decision was made for additional radiation therapy. Subsequently the patient developed cough with shortness of breath requiring admission to the hospital. He was initially empirically treated with Piperacillin/Tazobactam. Later his antibiotic regimen was expanded to vancomycin, meropenem and clarithromycin. However despite expansion in antibiotic coverage the patient developed progressive respiratory distress requiring transfer to the intensive care unit (ICU). Chest X ray at the time of admission revealed right lower lobe consolidation (Figure-1). The patient was noted to have leukopenia in the ICU and required intubation within 24 hours of admission. His labs during ICU stay were as follows; WBC ranged from $1.33 \times 10^3/\mu\text{l}$ to $5.42 \times 10^3/\mu\text{l}$, with Lymphocytes ranging from 0.16% to 0.75% and Neutrophils ranging from 1.07% to 5.15%; Haemoglobin ranged from 8.6 gm/dl to 10.7 gm/dl; Serum Creatinine 2.1

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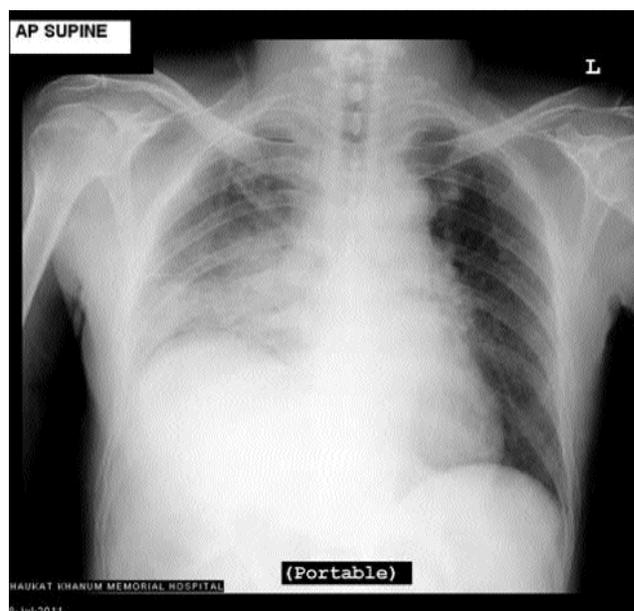


Figure-1: Chest X-ray at admission showing right lower lobe consolidation.

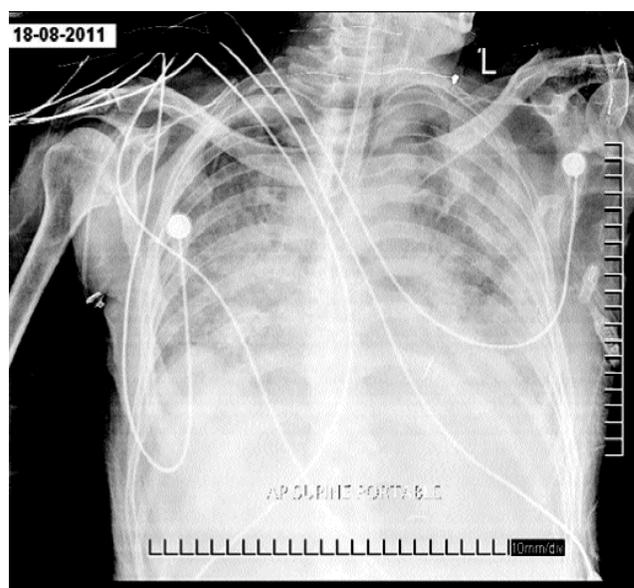


Figure-2: Last X-ray done in ICU showing worsening bilateral infiltrates when compared to that on admission.

Table: Laboratory results of patient.

Variables	Results
IgG (700-1600 mg/dl)	152.6mg/dL
IgA (70-400 mg/dl)	24.4 mg/dL
IgM (40-230 mg/dl)	7.6 mg/dL
CD4 cells (455-1502 cells/microliter)	23cells/microliter
CD8 cells (266-876 cells/microliter)	128 cells/microliter

mg/dl to 2.86 mg/dl, Rest of the electrolytes were within normal limits. On the sixth day of ICU stay the patients tracheal aspirate cultures grew aspergillus for which he was started on Amphotericin B. Given his leukopenia and failure to improve the suspicion of Good syndrome was raised and serum immunoglobulins levels were checked and found to be low with a reversal of the patients CD4/CD8ratio (Table-1). Based on these findings he was treated with intravenous immunoglobulin's for Good syndrome during his stay in ICU. The patient received a total of four days of immunoglobulin therapy but despite treatment the patients' condition worsened with the development of bilateral pulmonary infiltrates and severe sepsis (Figure-2). He subsequently expired secondary to multi organ failure.

Discussion

Good syndrome (immunodeficiency with concomitant thymoma) is a rare cause of combined B- and T-cell immunodeficiency in adults.¹ In 1954, Good first reported a patient with thymoma and co-existent hypogammaglobulinemia.³ Since that time our understanding of this syndrome has improved considerably and the approximate occurrence in patients with thymoma is estimated to be 3 to 6%.³ Good syndrome is among the long list of immunodeficiency differentials which include immunodeficiency due to HIV/AIDS, X linked agammaglobulinaemia (XLA), Autosomal Recessive Agammaglobulinemia, Selective IgM Deficiency, Selective IgE Deficiency, Antibody Deficiency with Transcobalamin II Deficiency, Drug-Induced Antibody Deficiency, Interferon- α /IL-12 Pathway Deficiencies, Natural Killer Cell Deficiency, Phagocyte Killing Defects, Specific Granule Deficiency. The clinical scenario in our patient favoured Good Syndrome. Patients with Good syndrome usually present in the 4th or 5th decade of life, and the frequency in males and females is similar. The immunodeficiency may precede or follow the diagnosis of a thymoma,³ but the immunologic abnormalities cannot be corrected by corticosteroid treatment or thymectomy.⁴ Although the cause and pathogenesis of this disorder are unknown, its main characteristics are hypogammaglobulinemia, a low B-cell

count or the absence of B cells, CD4+ T-cell lymphopenia and reduced serum levels of IgG, IgA, and IgM.⁴ A reduced mature B-cell count in bone marrow has also been reported.⁵ Since cell-mediated immunity is compromised, individuals with Good syndrome are susceptible to bacterial infections, particularly infections with encapsulated organisms, and opportunistic viral and fungal infections. Tarr et al.³ reported that sino-pulmonary infection with Haemophilus influenza was the most common infectious disease among 51 patients with immunodeficiency and thymoma. Other infectious diseases present in their patients were CMV, Pneumocystis jirovecii, infectious diarrhoea, and tuberculosis. Although systemic fungal infections are not characteristic of Good syndrome, mucocutaneous candidiasis has been documented in 24% of cases.⁴ Aspergillus is a rare cause complicating Good syndrome and a recent review of 152 Good syndrome cases revealed only 4 cases of aspergillus infections.^{1,9,11} In our case, given the overall critical condition of the patient, transbronchial lung biopsy could not be performed to confirm invasive aspergillosis. The possibility thus remains that the aspergillus isolated in our patient was a contaminant. However given the critical nature of the patient's condition, the culture results could not be ignored and antifungal treatment was initiated.

Autoimmune diseases such as myasthenia gravis, pure red-cell aplasia, pernicious anaemia, diabetes mellitus, and idiopathic thrombocytopenia may also be concomitantly present in these patients.² The treatment of patients with Good syndrome includes resection of the thymoma and immunoglobulin replacement to maintain adequate IgG levels. Immunoglobulin therapy helps prevent infections, reduces the duration of hospitalization and decreases the quantity of antibiotics needed to treat these patients.^{3,6,7} A retrospective review of the efficacy of immunoglobulin replacement for Good syndrome showed that 23 of 30 patients had favourable responses during their follow-up periods.³ However, there are no other established treatment options to suppress infections. According to a follow-up report,³ 29 of 50 Good syndrome patients subsequently died. Hermaszewski et al. reported that the 5- and 10-year survival rates were 70 and 33%, respectively.⁸ As high mortality is associated with this condition it is imperative that clinicians should have a high index of suspicion for diagnosing Good syndrome in patients with thymoma so that immunoglobulin therapy can be initiated.

Conclusion

This case illustrates the potential for severe infections with Good syndrome. Although this is rare, it is a predictable

cause of severe infections in thymoma patients. Recognition of this syndrome is critical to institution of immunoglobulin therapy and possible improvement of mortality or morbidity. Therefore thymoma patients with leukopenia or severe infections should have their immunoglobulin levels, CD4/CD8 ratio and B cell counts checked. This case also highlights the importance of placing these patients on broad spectrum antimicrobials including anti-fungals from the very beginning given the potential for fungal infections as demonstrated in our patient.

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