

Good's Syndrome – Nothing Good About It

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This report has never been presented anywhere.

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ABSTRACT

We report a rare case of Good's Syndrome (GS) or thymoma with immunodeficiency in a 48-year-old male patient. This condition presents in fourth or fifth decade of life. GS should be suspected in a person presenting with recurrent bacterial infections with encapsulated organisms and opportunistic viral and fungal infections in the setting of thymoma, hypogammaglobulinemia and reduced or absent B cells. Our patient presented with chronic diarrhoea for the past three years, repeated esophageal candidiasis and a superior anterior mediastinal mass. Duodenal biopsy showed CMV duodenitis. Lab investigations revealed low IgM levels [hypogammaglobulinemia] and the biopsy from the mediastinal mass was consistent with thymoma. This case is being written to highlight that unexplained repeated opportunistic microbial infections should prompt the clinician to suspect immunodeficiency in the background of a negative HIV status and to emphasize that GS is one of the causes of adult onset immunodeficiency where early recognition and treatment can improve and alter the course of the disease as GS carries a worse prognosis compared to XLA [X-linked agammaglobulinemia] and CVID [common variable immunodeficiency].

INTRODUCTION

GS or thymoma with immunodeficiency is a rare clinical entity first described by Dr Robert Good in 1954.^{1,2} Thymomas are slow growing relatively uncommon tumours associated with myasthenia gravis, autoimmune disorders and other chronic diseases such as hypertension, diabetes mellitus, renal insufficiency and coronary artery disease.² Acquired immunodeficiency or GS is one of the parathymic syndromes seen in fourth and fifth decades of life characterized by hypogammaglobulinemia in the setting of thymoma.² Patients present with recurrent sinopulmonary infections, chronic non-infectious diarrhoea and opportunistic infections.³ Reduced or absent B cells, decreased T cells, inverse ratio of CD4 +/CD8 + T cells and impaired T cell mitogen proliferative responses are the abnormal immunologic findings in GS.¹ A high level of clinical suspicion and in depth evaluation is required for the diagnosis of GS. Management of GS includes thymectomy and immunoglobulin replacement. The prognosis of GS is worse than XLA and CVID.^{1,3} It is noted that the 5-year survival rate of GS is 70% whereas XLA and CVID is nearly 100%.^{1,3} The 10-year survival rate declined to 33% in GS as compared to 95% in XLA and CVID.^{1,3,4} Infections, autoimmune diseases and hematologic complications are the principal causes of

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morbidity and mortality in patients with GS rather than thymoma itself.³

CASE REPORT

A 43-year-old male patient presented with chronic diarrhoea for 3 years associated with abdominal pain and distension and significant weight loss (loss of 14 kilos in 2 years). Diarrhoea was watery not associated with blood or mucus. He had travelled abroad seeking medical treatment for his symptoms. Hospital workup showed esophageal candidiasis, throat swab positive for *Candida* species and negative *Clostridium difficile* toxin. With the above clinical details, the patient was subjected for a repeat OGD (oesophagogastroduodenoscopy) and CT abdomen. Esophageal brushings and duodenal biopsies were obtained to rule out candida and celiac disease respectively. CT abdomen showed dilated small bowel loops with air-fluid levels and distended colonic segments with the radiological features suggestive of colitis and developing toxic megacolon. Hepatobiliary system showed dilated CBD (common bile duct) with internal septations, distended gallbladder and mild prominent biliary channels possibly representative of cholangitis. Routine blood tests showed mild decrease in hemoglobin 11.1 g/dL, increased eosinophils $1.1 \times 10^9/L$ and abnormal PT (17.3s) and APTT (42.1s). LFT (liver function test) showed raised ALT and AST. Further tests like immunoglobulin (Ig) levels, HIV status, tumour markers, liver autoantibodies, celiac screening and CMV PCR (cytomegalovirus polymerase chain reaction) were done. Meanwhile, CT chest was done which showed an enhancing soft-tissue lobulated mass in the superior anterior mediastinum measuring 6 x 9 x 8 cm [APxTVxCC] with areas of necrosis and curvilinear and punctate calcifications adhering to the ascending aorta and anterior part of the aortic arch compressing the left brachiocephalic vein suggestive of thymoma or thymic carcinoma (Figure 1). Paratracheal lymph nodes and a tiny subpleural pulmonary nodule were noted in the posterior segment of the left lower lobe. Test results showed normal tumour markers, negative for liver autoantibodies and celiac disease screening with low levels of IgM (less than 0.25). HIV negative.

Esophageal brushing cytology was positive for candidiasis. Duodenal biopsy was positive

for CMV inclusions (Figure 2) and negative for celiac disease. Correlating with the above clinical features (chronic diarrhoea) and test results such as low IgM, a mediastinal mass, repeated candidiasis and CMV colitis, Adult onset immunodeficiency syndrome: Good's syndrome was suggested in the histopathology report. Duodenal aspirate was negative for AFB (acid fast bacilli). Later, the patient was subjected for CT-guided aspiration and biopsy from the mediastinal mass. We received samples for cytology and histopathology. Microscopic examination showed thick fibrocollagenous capsule adjoining the nodular aggregates of cells comprising of benign polygonal epithelial cells with round nucleus, fine even chromatin and inconspicuous nucleoli along with few spindle epithelial cells. Benign lymphocytes were closely intermingled between these cells (Figure 1). No atypia or mitoses were seen. IHC showed epithelial cells strongly positive for CK19 and p63 with occasional CK 14 positive cells. Lymphoid cells were CD3 and TdT positive (Figure 2). With the above microscopic and IHC findings a histopathological diagnosis of thymoma type B2 was rendered.

Cytologic smears and cell block showed dimorphic population of cells (polygonal and spindle) along with lymphocytes similar to the histologic findings. The patient denied any further management at our hospital and preferred treatment elsewhere. No follow-up information is available as the patient has not turned up at our hospital.

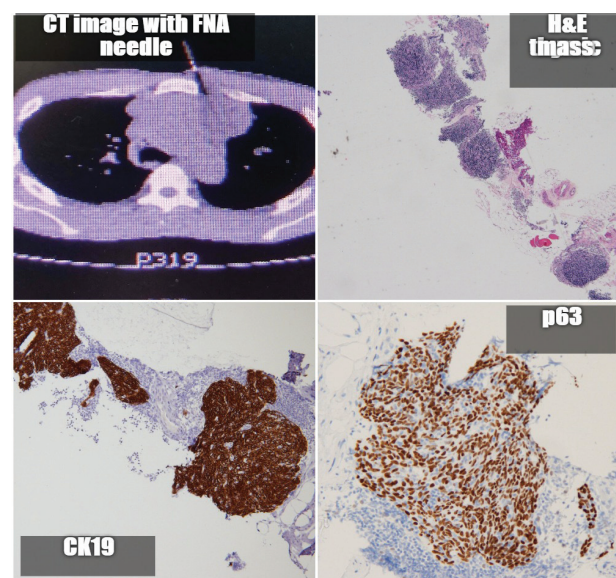


FIGURE 1. CT image with FNA needle in the thymic mass (upper left), core biopsy from thymic mass (H&E x 10x, upper right), CK19 IHC stain (lower left) and p63 IHC stain (lower right).

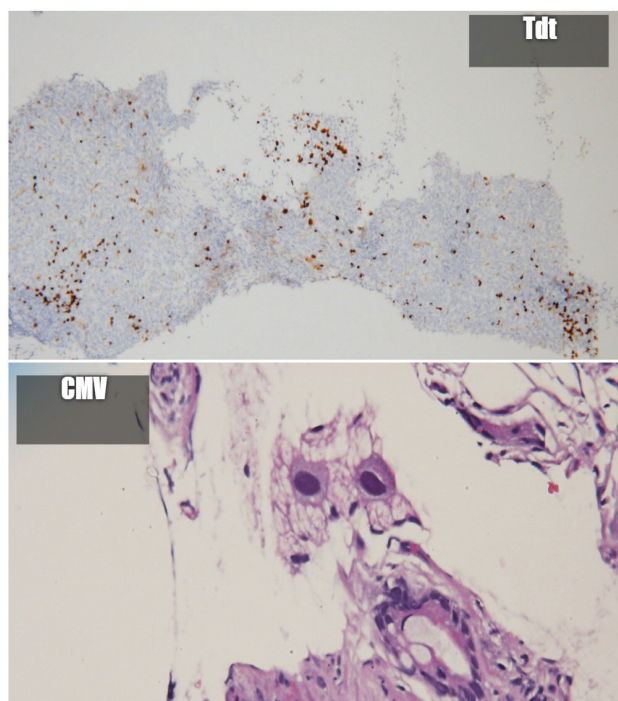


FIGURE 2. Tdt positive lymphocytes, IHC stain (upper image) and CMV intranuclear inclusions in the duodenal epithelial cells (H&E x 40x, lower image).

DISCUSSION

The rarity of GS and its variable presentation have created difficulty in clinical studies. WHO and International Union of Immunological Societies on primary immunodeficiencies have classified GS as a distinct entity even though no well-defined diagnostic criteria are available.¹ Two categories have been described. Classical GS, patients with thymoma and hypogammaglobulinemia and Probable GS, thymoma or thymic carcinoma and any unclassified ID.⁵ It is usually seen in adults in their fourth or fifth decades of life. GS in children is extremely rare, and one study showed the youngest GS patient aged 11 years.⁵ Hypoglobulinaemia shows decreased levels of serum IgG, IgM and IgA although cases with normal IgA have been reported.¹ Both cellular and humoral components of immunity are affected in GS.² Sinopulmonary infections by encapsulated organisms is the common symptom.¹ This is seen XLA, CVID and

GS. Diarrhoea is seen in 50% of the patients. The common pathogens isolated are enteric bacteria, Giardia and CMV, although most cases are negative for any kind of pathogen where inflammatory colitis is thought to cause diarrhoea similar to that seen in CVID.¹ Bacterial urinary tract infections, skin infections and rare arthritis have been reported in GS patients.¹ GS patients suffer from opportunistic infections associated with disorders of cell mediated immunity unlike in patients with XLA and CVID.¹ 87% of cases showed reduced or absent B cells and 45% cases with reduced T cell mitogen responses.^{1,2} Although no specific etiology is known, evidence of a basic defect in the bone marrow is suggested.¹ Precursor B-cell growth and differentiation are inhibited by a cytokine produced by the bone marrow stromal cells.⁴ T cells isolated from thymoma inhibits immunoglobulin (Ig) production by B cells and pre-B cell growth in the healthy controls.¹ The diagnosis of GS is clinically challenging with a high index of suspicion for immune deficiency. Repeated infections of the sinopulmonary and GI tract and opportunistic bacterial, viral and fungal infections in the absence of HIV should alert the physician for a detailed immunological workup.³ Treatment involves thymectomy and IV immunoglobulin replacement along with specific antimicrobial prophylaxis (HSV and Pneumocystis) and appropriate vaccinations.² Long-term prognosis depends upon the completeness of tumour excision (thymoma).¹ Study by Jansen et.al, showed a median survival of 14 years.⁵ Immunoglobulin replacement should be monitored with serum levels.² Our case presented with chronic diarrhoea for three years, recurrent esophageal candidial infection and an anterior mediastinal mass. Lab investigations showed low IgM, CMV duodenitis and mediastinal mass consistent with thymoma. It was not possible for a detailed immunological workup as the patient refused any kind of further management at our hospital.

CONCLUSIONS

GS [thymoma with immunodeficiency] is a rare condition of adult onset immunodeficiency with combined B and T cell immunodeficiencies. Recurrent infections in a patient including infection by opportunistic microbes should alert the clinician for a detailed immunological

workup of the patient. Conversely, in all patients with thymoma immunological workup and quantitative immunoglobulin assay should be included as a part of their routine diagnostic evaluation. Morbidity and mortality depends on the severity of infections and are influenced by the presence of associated hematologic derangements and autoimmune diseases. Though, no specific protocols are available for treatment of GS, effective management by thymectomy, immunoglobulin repletion, the identification of infecting microbe, targeted antimicrobial prophylaxis and appropriate vaccinations can alter the course of the disease. This multifaceted approach will be able to keep the patient symptom free. Our case with chronic diarrhoea, weight loss, repeated opportunistic infections and low Ig M levels underwent a chest CT which led to the discovery of a mediastinal mass finally proven as thymoma. Thymoma with immunodeficiency - Good's syndrome.

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