A 22-Year-Old Woman With Bronchiectasis and a Mediastinal Mass

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A 22-year-old woman presented to the ED following several days of worsening shortness of breath and chest tightness associated with tachypnea and palpitations. Her past medical history was significant for several months of nausea and vomiting, crampy abdominal pain, intermittent loose stool, and weight loss. Severe gastritis and pyloric ulcers were discovered during an upper endoscopy approximately 1 month prior; she was treated with a proton pump inhibitor and sucralfate. She had previously been healthy and did not have a history of alcohol consumption, smoking, or intake of nonsteroidal antiinflammatory drugs. Her initial chest radiograph and chest CT scan are shown in Figures 1 and 2. She denied frequent respiratory illness as a child.

Physical Examination Findings

On physical examination the patient was afebrile, with a heart rate of 113 beats/min, BP of 101/65 mm Hg, respiratory rate of 22 breaths/min, and oxygen saturation of 99% on room air. Neck examination revealed no thyromegaly, jugular venous distention, or cervical

FIGURE 1. Posteroanterior chest radiograph demonstrates upper lobe predominant scarring, architectural distortion, and subtle cystic and cylindrical bronchiectasis. Contour deformity of the right upper mediastinum with silhouetting of the ascending aortic contour represents an anterior mediastinal mass.

lymphadenopathy. Cardiac examination was notable for tachycardia. Bilateral inspiratory crackles were noted on lung auscultation. On abdominal examination she had diffuse mild tenderness to palpation

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FIGURE 2. A, Representative axial CT image displayed with lung window settings demonstrates architectural distortion and bilateral cystic and cylindrical bronchiectasis in the upper lobes and superior portion of the lower lobes. B, Mediastinal window demonstrates a 5.6 × 2.3-cm soft tissue mass with small calcifications in the anterior mediastinum abutting the ascending aorta.

without organomegaly. The rest of the physical examination was unremarkable.

Laboratory Findings

Laboratory findings showed a normal chemistry panel and normocytic anemia (hemoglobin = 10.4 g/dL). Thyrotropin and free T4 levels were normal. Serum immunoglobulin levels showed IgG 354 mg/dL (normal, 694-1,698 mg/dL), IgA 40 mg/dL (normal, 63-378 mg/dL), and IgM 19 mg/dL (normal, 60-263 mg/dL). HIV test was negative. A bronchoscopy with BAL and transbronchial biopsy did not isolate any organisms and showed normal lung parenchyma.

*What is the next diagnostic step?*⁹

*What is the probable diagnosis?*⁹

Next diagnostic step: Biopsy of the mediastinal mass

Diagnosis: Good syndrome

DISCUSSION

Good syndrome was first described by Dr Robert A. Good in 1955. Good was a pioneer in modern immunology and performed the first successful bone marrow transplant. Good syndrome is classified as a distinct entity by the World Health Organization/International Union of Immunologic Societies expert panel on immunodeficiencies, although no formal diagnostic criteria exist. Most define Good syndrome as the presence of a thymoma in the setting of hypogammaglobulinemia. Good syndrome is rare, with only about 155 cases reviewed in the English literature. With a worldwide distribution, the condition has an equal prevalence in men and women. Although symptoms most commonly present between the fourth and fifth decades (average 59.1 years), onset varies widely from 8 to 90 years old. In one study of adults with primary antibody deficiency attending chest clinics, Good syndrome was present in 7% of cases. However, this figure likely represents a referral bias; actual rates in those requiring immunoglobulin replacement therapy are closer to 1% to 2%.

Good syndrome is characterized by thymoma, adult-onset immunodeficiency, decreased or absent peripheral B cells, variable defects in cell-mediated immunity, CD4⁺ to CD8⁺ T-cell ratio inversion from the normal ratio of 2.0, and reduced T-cell mitogen proliferative responses. The cause of these immune deficiencies in Good syndrome remains elusive. Several theories have been proposed, including cytokine-induced B-cell maturation arrest in the bone marrow and loss of either naive or memory CD4⁺ T cells. Given the prevalence of autoimmune abnormalities associated with Good syndrome, the loss of B-cell function may also represent an autoimmune destructive process.

The clinical presentation of Good syndrome varies. Some asymptomatic patients present with an incidentally detected anterior mediastinal mass. Others have symptoms secondary to the mass effects of the thymoma, such as dyspnea and chest pain, myasthenia gravis, or Horner syndrome, or present with recurrent infections resulting from the associated immune deficiency.

Most thymomas associated with Good syndrome are 2004 World Health Organization type A or type AB (41.7%). Type B2 thymoma, such as seen in this patient, is the second most prevalent type in Good syndrome and is associated with 25% of cases. Diagnosis may actually precede immunologic symptoms by many months to years. The most common symp-

toms associated with the anterior mass include cough, dysphagia, and hoarseness. The mass may also be asymptomatic and be an incidental radiologic finding.

Patients with Good syndrome have increased susceptibility to bacterial, viral, and fungal pathogens due to humoral and cell-mediated immune deficiency. Recurrent sinopulmonary infections are most commonly seen, and it is not unusual for patients to develop bronchiectasis, such as seen in this patient. Good syndrome also increases risk for opportunistic infections; cytomegalovirus and *Candida* species are most commonly reported.

Despite the overall low levels of immunoglobulins, 30% to 58% of patients will have complications resulting from development of autoantibodies. Pure red cell aplasia is the most common manifestation of autoantibody disease, followed by myasthenia gravis. Although not completely understood, chronic diarrhea, as exemplified by this patient, is also a common symptom associated with Good syndrome and is described in 39% to 50% of cases. Infectious organisms are isolated in only a minority of cases, leading to speculation that there is an autoimmune basis of the diarrhea, similar to the colitis seen with common variable immune deficiency.

Treatment consists of surgical removal or debulking of the thymoma. Patients with locally advanced-stage disease and/or metastatic disease may also require radiotherapy or combination chemotherapy. Removal of the tumor usually has favorable effects on the autoimmune disorders associated with Good syndrome, such as myasthenia gravis and pure red cell aplasia. Unfortunately, it does not seem to reverse the serum immunologic abnormalities, which can present months to years after tumor removal. Treatment with IV immunoglobulin is indicated in patients with hypogammaglobulinemia and can improve infection control and decrease hospitalizations. Bronchiectasis often develops because of recurrent sinopulmonary infections. Those who develop significant bronchiectasis should be followed closely by a chest physician and may require chronic treatments, such as postural drainage and prophylactic antibiotics, along with immunoglobulin replacement. The overall prognosis for Good syndrome remains worse than that for other immune deficiencies, with causes of death including infections, autoimmune disease, and hematologic complications. Patients requiring immunosuppression because of the presence of concomitant autoimmune disease usually have a more severe course.

Clinical Course

The patient underwent median sternotomy with resection of the anterior mediastinal mass. The pathology (Fig 3) was consistent with a type B2 thymoma,

FIGURE 3. A, World Health Organization type B2 thymoma composed of polygonal neoplastic cells with prominent nucleoli and admixed smaller lymphocytes (hematoxylin and eosin, original magnification $\times 200$). B, Tumor invading into the lung parenchyma (hematoxylin and eosin, original magnification $\times 40$).

which confirmed the diagnosis of Good syndrome in the setting of her hypogammaglobulinemia. She required en bloc resection of the thymus gland, pericardium, and portion of the right upper lobe because of invasion of the right upper lobe visceral pleura and pericardial adipose tissue. She continued to have intermittent abdominal pain and anorexia, but this improved with time, and she is well nearly 2 years after the initial presentation.

CLINICAL PEARLS

1. *Good syndrome, a rare occurrence of immunodeficiency and thymoma, should be considered whenever a thymoma is diagnosed, as the incidence of associated hypogammaglobulinemia is up to 11%.*
2. *In patients who develop Good syndrome, the immunologic deficiencies may precede the diagnosis of the thymoma by months or years.*

3. *Good syndrome is a disorder of both humoral and cellular immunity, with associated susceptibility to opportunistic infections.*

4. *Treatment of the thymoma may improve associated autoimmune disorders but often does not reverse the serum immunoglobulin deficiencies.*

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