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Good Syndrome Associated with Organizing Pneumonia

Short communication

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Short Communication

The Good's Syndrome (GS) is a rare disease, observed in of patients with primary antibody deficiency who are on immunoglobulin replacement treatment [1]. GS can present with a constellation of symptoms ranging from local disorders due to the thymoma, itself (such as cough, chest pain, dysphagia, dyspnea, superior vena cava syndrome, Horner's syndrome), to systemic manifestations including autoimmune disease (giant cell myocarditis, myasthenia gravis) and finally also to recurrent infections. These are due to defects in humoral and cellular immunity associated with a thymoma [1]. Moreover, anemia is seen in 50 to 86% of patients, with Pure Red Cell Aplasia (PRCA) being the most common cause, along with aplastic, hemolytic, and pernicious anemia and myelodysplastic syndromes. These manifestations are indicative of bone marrow failure and bone marrow dysfunction may be responsible for other hematologic defects associated with GS including lymphocytopenia, CD4 lymphopenia, neutropenia and eosinopenia [2].The syndrome occurs equally in females, and male and it may appear at any age, although it typically occurs between 4th or 5th decade of life [1].

Although a clear pathogenic model of GS remains unclear [2] GS is traditionally grouped with antibody deficiencies, whereas 100% GS patients have low serum IgG levels and 86% have low IgA and 93% low IgM. GS patients lack B cells, suggesting a defect or interference in lymphopoiesis during early B cell development [2]. Most B cell progenitors (BCPs) of GS arrested at the earlier Pro-B cell stage [3]. Several studies have shown that the thymic tumor microenvironment can cause aberrant maturation of T cell precursors and alter the T cell subset composition in the blood, although most studies are limited to myasthenia gravis [3]. No disease-causing variants have been associated with GS [4] GS may not be driven by a mono or polygenic cause [2], however the studies have not determined the roles of incomplete penetrance or mosaicism. Understanding the mechanism of disease in GS may also shed light on the role of age-dependent epigenetics in B cell lymphopoiesis [2-4].Treatment of Good's syndrome involves resection of the thymoma and immunoglobulin replacement to maintain adequate trough IgG values [1].

We herein present a case of a 49-year-old patient in usual good health conditions who was, recently, hospitalized for community acquired pneumonia successfully treated with clarithromycin and co-amoxicillin. A non-productive cough and feverish rises were persisting after hospital discharge and two weeks later she was, therefore, admitted to the Emergency Department, where blood cultures and infectious tests (rapid COVID test, influenza/RSV smear, smear and PCR for Mycoplasma pneumoniae, Chlamydophilia pneumoniae, Legionella) were negative. Blood works were characterized by normal blood cell counts, markedly elevated ESR and CRP, and by an inflammatory serum protein electrophoresis. A chest CT scan showed bilateral infiltrates, so it was decided to carry out further investigations via bronchoalveolar lavage which gave a positive result for SARS-CoV2 infection and showed an increased but aspecific cellularity. At this time, nasopharyngeal smear for SARS-CoV2 turned positive. Consensually the chest CT revealed a rounded mass affecting the anterior mediastinum. She was treated with oxygen therapy, oral dexamethasone and remdesivir.

The course was favorable as the patient could be quickly weaned from oxygen therapy. However, the persistence of subfebrile temperature, lung base hypophonesis and migrating infiltrates on CT chest were leading to the suspicion of organizing pneumonia. Pulmonary function tests (PFTs) revealed moderate restriction and reduction in diffusion capacity. Therapy was instituted with prednisone at 50 mg daily. She experienced significant clinical improvement over the next few months. An extensive autoimmune work-up was negative for ANA, pANCA, cANCA, CCP antibodies, dsDNA antibodies, RF, and anti-RO (SSA) and anti-LA (SSB) antibodies. Serology for hepatitis B, hepatitis C, EBV, CMV and HIV was negative. The immunological balance performed shows hypogammaglobulinemia (IgG 2,24g/L, IgM 0.19g/L, IgA 0.24g/L), with a profound depletion of CD19 and relative depletion of CD4 (317 cells/ul): picture suggestive for a combined de-

ficiency (humoral and cellular). Vaccination responses, unfortunately, have not been determined, as the patient has promptly started replacement with IVIG (0.4g/kg/month). She denies sinopulmonary or opportunistic infections in childhood when she underwent a vaccination schedule according to the local guidelines.

T cell proliferative responses to PHA and interleukin 2 (IL-2)/OKT3 will be performed in the next future. .Abdominal CT scan was negative. A PET-CT has been scheduled for oncology management and thymectomy discussion. The diagnosis of GS in our case was based on a medical history. The presence of bilateral lung infiltrates and mediastinal lymphadenopathy raised initially the suspicion for either an infectious process or lymphoproliferative disorder. Also a granulomatous disorder was in the differential. Thus the diagnostic procedure must include a histological specimen. The diagnosis of GS can be difficult. Various presentations associated with this syndrome can occur during different periods, sometimes with intervals of several years. The different signs and symptoms may not initially be interrelated. The GS can be easily missed especially because of its protean manifestations of autoimmune and parathymic syndromes. It is crucial that once a diagnosis of thymoma is made, a thorough history and evaluation with longitudinal follow-up and surveillance be done to rule out various syndromes associated with this condition [5,6].To our knowledge, this is the first case of GS associated with organizing pneumonia (OP). The OP refers to a non-specific response to an initial injury to bronchial epithelium.

These initial insults can be from inhalational injury, infections or drug exposures. OP is called cryptogenic OP when it is idiopathic. Histologically this disorder is characterized by excessive proliferation of granulation tissue consistent with loose collagen-embedded fibroblasts and myofibroblasts. Plugs of granulation tissue are found in alveolar ducts and alveolar spaces with or without bronchiolar intraluminal polyps. Inflammatory cells, mainly lymphocytes and plasma cells, are commonly found in the interstitium. BAL typically reveals an increase in all cell types with lymphocyte prevalence. OP is clinically characterized by a subacute illness with dyspnea, cough, fever, malaise and weight loss. A typical pattern of bilateral patchy alveolar infiltrates is seen on chest CT scan.

PFTs reveal a mild-to-moderate restrictive defect. The histological diagnosis can be made by transbronchial lung biopsy but open lung biopsy might be sometimes required as diagnosis can be missed on small specimens. The exact pathogenesis of OP itself remains not well-defined. It is thought that OP is a consequence of epithelial injury that leads to leakage of plasma proteins, recruitment of fibroblasts and fibrin formation within the alveolar lumen. Also dysregulation of vascular endothelial growth factor and matrix metalloproteinase has been associated with OP. One could speculate on the presence of a pathogenetic relationship between the COVID infection and the initial epithelial lung injury that leads to OP. Once the diagnosis was established, corticosteroid therapy was promptly instituted and resulted in dramatic clinical, and radiographic response [7,8]. Further studies on a larger number of patients are needed to confirm our findings and to better address the pathophysiological basis of GS [1].

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