THE NEW ZEALAND MEDICAL JOURNAL
Vol 117 No 1188 ISSN 1175 8716

Thymoma and immunodeficiency

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Good syndrome (GS) was first described in 1954 by Good, who reported hypogammaglobulinaemia in a small percentage of patients with thymoma.[1] GS is a rare, adult-onset, immunodeficiency disease characterised by hypogammaglobulinaemia, low or absent B cells in the peripheral blood and, variably, defects in cell-mediated immunity.[2] GS was often considered a subset of common variable immunodeficiency (CVID) with thymoma, whereas nowadays it is regarded as a distinct clinical entity whose pathogenesis is still uncertain.[3] A bone marrow defect impairing B cell maturation due to an aggression towards B cell precursors has been suggested,[4] and deficiencies in other cell lineages with eosinopenia, pure red cell aplasia or neutropenia are often reported.[5]

Here we report the case of a male patient who developed recurrent respiratory tract infections for two years before being diagnosed with GS.

Case report

A 61-year-old male presented in March 1996 with a two-year history of recurrent respiratory infections including otitis, bronchitis, sinusitis and two episodes of pneumonia. Chest X-ray and chest CT scan showed a mediastinal mass, biopsy of which revealed lymphoid cells.

The mass was resected in June 1996 and histopathologic examination showed a mixed epithelial and lymphocytic thymoma with infiltration of the capsule. The patient had low serum levels of IgG (24 mg/dl, normal >700), IgM (5 mg/dl, normal >40) and IgA (5 md/dl, normal >70). The total number of lymphocytes was normal, but the CD4+ T cell count was 420 per ul, with an inverted CD4/CD8 ratio of 0.39 and absent peripheral B cells. PPD skin reactivity was positive. A serological test for HIV was negative.

Two months after thymectomy, he developed pneumonia due to *Serratia marcescens*, which resolved with antibiotics. Monthly intravenous immunoglobulin (IVIG) infusions were started at a low dosage (150 mg/kg) and the patient improved slightly. In August 1998 he presented with oral thrush, odynophagia, and a weight loss of 7 kg. Upper gastrointestinal endoscopy revealed *Candida oesophagitis*, which was treated with itraconazole. Cough and sputum production persisted. In April 2000 *Haemophilus influenzae* type B was isolated from sputum and the patient was treated with a 15-day course of ceftriaxone. The dosage of IVIG infusion was increased (400 mg/kg every three weeks) and the patient experienced a gradual improvement in his condition, with decreased sputum and cough and fewer febrile episodes. A recent chest CT scan did not show bronchiectasis.

He continues to take daily itraconazole in spite of which he occasionally develops oral candidiasis, which resolves with local nystatin treatment. In 2000 and 2001 immunological evaluation was repeated: CD4+ T cells were still reduced with an

inverted CD4/CD8 ratio. In vitro lymphocyte proliferation was normal. Intracellular IL2 and IFN-γ cytokine production was normal. He also has mild neutropenia (1200/mm^3).

Discussion

GS was one of the first immunodeficiency diseases to be classified.[1] Patients with GS are usually middle-aged or elderly when they develop recurrent infections, most frequently of the respiratory tract. It is usually the infections rather than the local symptoms due to the mediastinal mass that call attention to the possibility of thymoma. Only 3–6% of patients with thymoma are, however, hypogammaglobulinaemic and the relationship between thymoma and the immune dysfunction is not clear;[6] thymoma does not seem to induce hypogammaglobulinaemia because after it is surgically removed the immune impairment persists, as in our patient who, after thymectomy, continued to be hypogammaglobulinaemic.

The deficient humoral immunity in GS is the main cause of the recurrent respiratory infections, with an overall spectrum of manifestations and pathogens similar to other hypogammaglobulinaemic conditions, such as CVID.[7] However, in GS opportunistic infections, such as mucocutaneous candidiasis (as seen in our patient), herpes zoster, *Pneumocystis carinii* pneumonia and recurrent herpes simplex virus infections develop more frequently than in CVID.[8] The occurrence of opportunistic infections in GS seems to be due to defects in cell-mediated immunity, which have been found in several patients.[9] In our patient, CD4+ T cells were reduced with an inverted CD4/CD8 ratio but he also had a mild neutropenia, which may also contribute to the recurrence of mycotic infections.

Several haematological disorders have been reported in GS, including pure red cell aplasia, pancytopenia, and autoimmune haemolytic anaemia.[5] The target in many of these disorders appears to be the stem cell committed to a haemopoietic lineage with loss of that lineage, even if the role of autoantibody-mediated mechanisms in the destruction of the lineage cannot be excluded.[9]

Finally, our case report confirms the importance of IVIG replacement in GS at appropriate doses in order to improve the control of infections and perhaps prevent the development of bronchiectasis,[10] which to date has not been identified in our patient.

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