A patient with pure red cell aplasia and Good's syndrome

Sir,

Patients with thymoma sometimes exhibit concomitant autoimmune diseases, including pure red cell aplasia (PRCA). Moreover, some patients with thymoma developing one type of immunodeficiency like agammaglobulinemia are now designated as having Good's syndrome.1 Here we report a case of a patient with PRCA accompanied by Good's syndrome.

A 57-year-old man was admitted in July 1995 with palpitations on effort, edema of the legs, arms and face, but no hepatosplenomegaly. The laboratory findings showed a red blood cell count of 2.18×10^12/L, hemoglobin of 69 g/L, hematocrit of 0.201/L, serum iron of 58.9 µmol/L, total iron binding capacity of 62.0 µmol/L, ferritin of 1085 µg/L, and erythropoietin of 1690 mU/mL. Other hematologic and biochemical data were all normal. The bone marrow aspirate revealed absence of erythroid component (0%) without dysplasia of leukocytes or platelets (Figure 1A) and normal male karyotype by cytogenetics. He also had a mediastinal mass tentatively diagnosed as thymoma from the chest X-ray and computed tomograph, and hypogammaglobulinemia, including IgG of 2.11 g/dL, IgA of <0.333 g/dL, IgM of <0.298 g/dL and IgD of <0.1 g/dL. The surface antigen of lymphocytes from peripheral blood analyzed by flow cytometry demonstrated 40.7% of CD8+ cells as compared to 34.7% CD4+ cells, similar to another report.2 CD8++ cells expressed HLA-DR and lacked CD16, CD56, CD25, indicating no findings of granular lymphocyte proliferative disorders in which proliferated T cells suppressed erythropoiesis.3

Treatment with prednisolone (PSL) and cyclophosphamide (CPA) had no effect. Thus, extensive thymectomy with lymph node dissection was performed in October. The histologic diagnosis was epithelial cell predominant type thymoma. After temporary improvement of anemia before PSL tapering and no effects on the development of anemia with cyclosporin A, azathioprine or CPA in 1996, improvement of anemia was seen more than 50 days after starting treatment with PSL (1 mg/kg) in 1997 (Figure 1B). Although sulfamethoxazole, amphotericin B were given for infection prophylaxis, he suffered herpes zoster, repeated pneumonia, candidiasis and cytomegalovirus (CMV) retinitis and was treated with acyclovir, antibiotics, antifungotics and ganciclovir, respectively. Despite normalization of anemia, the serum IgG remained between 2.0-4.0 g/dL with periodic administration of immunoglobulins (CMV high titer). In 1999, his hemoglobin is still normal with PSL tapered to 5 mg.

To our knowledge, only 9 patients, including our patient, have been reported to have PRCA, thymoma, and hypogammaglobulinemia,2,5-8 however, no patient, except ours, was given a diagnosis of Good's syndrome. In our case, anemia improved in response to immunosuppressive agents as it did in most of the other cases,2,5-8 but an increased frequency of various infections was seen, since Good's syndrome is an immunodeficiency condition. Thymectomy normalized erythropoiesis in 1 out of 2 cases.7 However, the onset of PRCA was seen after resection in other 2 cases.7,8 The indications for treating PRCA by thymectomy, which yields no benefit to Good's syndrome,4 must be carefully determined. Our case highlights the strategic problems in treating patients with PRCA accompanied by Good's syndrome. We should keep in mind their immunodeficiency condition before and during therapy for PRCA.

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Key words
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Figure 1. Markedly decreased hemopoiesis in erythroid cells (A) was improved after administration of corticosteroid (B).
Leukemia and myelodysplasia in patients with essential thrombocythemia treated with cytotoxic agents

Sir,

Essential thrombocythemia (ET) is characterized by increased thrombohemorrhagic risk. Cytotoxic drugs are used in patients at high risk for thrombotic complications, while their use is still debated in low risk patients because of the risk of leukemia or secondary neoplasia. We describe the leukemic risk of available treatments in 187 consecutive patients (66 males and 121 females, mean age 51 ± 17 years) followed in our Department between 1985 and 1997 (median follow up 7 years, SE 2.3). Twenty-three patients received busulfan (BU, 2-4 mg/d), 1 associated with pipobroman (Pi, 25-50 mg/d), 6 radiophosphorus (32P, 74-185 M Bq), 48 hydroxyurea (HU, 10-30 mg/kg/d) in 62 cases associated with acetyl salicylic acid (ASA, 100 mg/d). Seventy-seven patients received ASA alone and 33 were not treated.

We observed 2 cases of non-lymphoblastic acute leukemia (AL) and 1 of chronic myelo-monocytic leukemia (MDS). No cytogenetic alteration was present in these patients at the time of the diagnosis. One patient evolved into AL, after a spent phase, 9 years after diagnosis of ET treated with BU (132 mg) and HU (414 gr). An 81-year old female was treated with HU (355 mg) and BU (185 mg) for ET and 3 years later developed MDS (Figure 1). They represented 23% of all patients treated with more than 1 cytotoxic agent and 16.6% of 32P treated subjects (incidence rate of AL/MDS in treated patients: 0.6/100 patients/years). The MDS represents 4% of cases of ET over 70 years of age (0.75 case/100 patients/years). No other case of spent phase was registered in our cohort of patients. No cases of AL or MDS were observed in patients without cytotoxic therapy (with or without ASA). Three patients developed cancers (1 colonic, 1 rhino-pharyngeal and 1 gastric). Only in one case did the patient receive 32P (74 M Bq) for ET, the others were under aspirin therapy.

The risk of leukemic transformation in patients treated with 32P appears to be highest between the 5th and 10th years and is usually preceded by a spent phase with myelofibrosis. Our case of AL after 32P therapy has these characteristics.