Pure Red Cell Aplasia Associated with Good Syndrome

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Pure red cell aplasia (PRCA) and hypogammaglobulinemia are paraneoplastic syndromes that are rarer than myasthenia gravis in patients with thymoma. Good syndrome coexisting with PRCA is an extremely rare pathology. We report the case of a 50-year-old man with thymoma and PRCA associated with Good syndrome who achieved complete PRCA remission after thymectomy and postoperative immunosuppressive therapy, and provide a review of the pertinent literature.

Key words: 1. Thymoma 2. Pure red-cell aplasia 3. Hypogammaglobulinemia

Case report

Thymoma is the most common primary neoplasm of the anterior mediastinum in adults. Approximately 40% of thymoma patients have clinically associated parathythic syndromes, with myasthenia gravis being the most common. Pure red cell aplasia (PRCA) is characterized by normocytic anemia, reticulocytopenia, and severe erythroid hypoplasia in the bone marrow without leukopenia or thrombocytopenia. Although PRCA occurs in only 5% of thymoma patients, thymomas are found in 50% of PRCA patients [1]. Good syndrome, in which thymoma is combined with hypogammaglobulinemia, occurs in approximately 6% to 11% of thymoma patients and is characterized by low serum immunoglobulin levels, a paucity of B cells, abnormal CD4+/CD8+ T cell ratios, and CD4 T cell lymphopenia [1,2]. PRCA is an extremely rare complication of Good syndrome. We report a case of PRCA associated with Good syndrome and review the reported cases of thymoma associated with these 2 paraneoplastic syndromes.

A 50-year-old man had been experiencing proximal muscular weakness since November 2011. He was a nonsmoker, and his medical history was unremarkable. Upon consultation, he underwent a computed tomography scan of the thorax, which revealed an anterior mediastinal tumor, 4.5 cm in diameter, with no evidence of having spread to adjacent tissue (Fig. 1). He was diagnosed with thymoma and also had hypogammaglobulinemia. His proximal muscular weakness resolved spontaneously, but his anemia became aggravated. Bone marrow aspiration was performed because of severe anemia and the absence of reticulocytes in the peripheral blood. The bone marrow specimen showed normal myeloid and megakaryocyte differentiation but no erythroid precursors; he was diagnosed with PRCA. He was referred to Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital for surgical anterior mediastinal tumor removal. The laboratory findings on admission included a red blood cell count of 210×10^6/μL, a
hemoglobin level of 6.3 g/dL, hematocrit of 18.4%, a mean corpuscular volume of 88 fl, a mean corpuscular hemoglobin of 30.0 pg, and a reticulocyte percentage of 0.3%; the leukocyte and platelet counts were normal. His blood chemistry was normal except for abnormally low serum total protein and albumin levels. His serum gamma globulin levels were extremely low, and he had an immunoglobulin G level of 343 mg/dL, an immunoglobulin A level of 16 mg/dL, and an immunoglobulin M level of 7 mg/dL. His serum anti-acetylcholine receptor antibody level was less than 0.2 nmol/L. After transfusion of 4 units of blood, he underwent extensive thymectomy via a median sternotomy. The tumor was noninvasive to the neighboring structures and was completely resected with the thymus. A pathological examination revealed Masaoka stage I and type AB thymoma (Fig. 1). His anemia and hypogammaglobulinemia did not resolve for 2 months after surgery; hence, cyclosporine A was administered at a daily dose of 4.4 mg/kg (300 mg); its trough concentration in the blood was 150 to 220 ng/mL. His hemoglobin levels increased after a month of immunosuppressive therapy. PRCA improved within 2 months after the therapy was initiated. However, his hypogammaglobulinemia did not resolve. The cyclosporine A dose was slowly tapered as PRCA resolved and a decline in renal function was seen, it was stopped completely in a year, and he is now being treated with intravenous gamma globulin infusions.

Discussion

Thymoma is an uncommon neoplasm derived from the epithelial cells of the thymus and is the most common tumor of the mediastinum in adults. The association between thymoma and autoimmune diseases such as myasthenia gravis, PRCA, and hypogammaglobulinemia has been long known. PRCA, first...
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characterized by Kaznelson in 1922, is defined by the absence of mature erythroid precursors in an otherwise normocellular bone marrow. PRCA can be a congenital disorder or an acquired syndrome. Acquired PRCA may occur with neoplastic disorders, including thymoma, and autoimmune diseases such as lupus erythematosus. Immunodeficiency complicated by thymoma, known as Good syndrome, was first described by Good [3] in 1954. Immunodeficiency in Good syndrome is characterized by the absence or low counts of circulating B lymphocytes, a marked decrease in all classes of immunoglobulins, and an abnormal CD4+/CD8+ T-lymphocyte ratio [4]. Most patients experience recurrent diarrhea and opportunistic infections of the respiratory tract, urinary tract, and skin. Hermaszewski and Webster [5] reported that the 5-year survival rate was 70% and that the 10-year survival rate was 33%.

The association of 2 or more paraneoplastic syndromes is rare. PRCA as a complication of Good syndrome is extremely rare. The definitive mechanism underlying the co-complications of thymoma, PRCA, and hypogammaglobulinemia remains to be clarified. Only a few reports have discussed the coexistence of PRCA and hypogammaglobulinemia in patients with thymoma. Only 16 patients, including our patient, have been reported with a clear postoperative course [6-8]. The reported patients comprise 9 females and 7 males, with a mean age of 57.9 years (standard deviation=10.2 years; range, 41 to 79 years). Complete resection was performed in 15 cases, except in 1 patient because of dissemination. Histologic classification according to the traditional and World Health Organization classifications identified 1 spindle cell thymoma, 1 epithelial cell thymoma, 1 lymphothymoma, and 3 type A, 6 type AB, 2 type B1, and 1 type B2 thymomas. The most common histologic type in co-complication with PRCA and Good syndrome was type AB. According to the Masaoka staging classification, 7 thymomas were stage I, 1 was stage II, 2 were stage III, and 1 was stage IV. Cases with Masaoka stages II, III, and IV and invasive thymoma were also observed. PRCA was treated by surgery and adjuvant therapy in 13 cases (81.3%); however, PRCA was only found to improve after surgery in 2 cases (12.5%). Adjuvant therapy using immunosuppressive agents may be necessary to achieve complete remission. The onset of PRCA was seen in 2 cases after surgery. Three-month postoperative cyclosporine treatment resulted in complete remission of PRCA in our case. Of the reported 16 cases, hypogammaglobulinemia resolved in 2 (12.5%). The onset of hypogammaglobulinemia was seen in 2 cases after surgery. Most case reports have stated that hypogammaglobulinemia in patients with Good syndrome did not improve after surgery followed by additional treatment such as immunosuppressive agents. Other treatment modalities have also been tried, such as plasmapheresis and splenectomy; however, these modalities yielded moderate results [8]. In our case, hypogammaglobulinemia did not resolve after surgery. Of the reported 16 patients, 2 died of infections. Extended thymectomy together with intravenous immunoglobulin infusion might be the treatment of choice for thymoma and hypogammaglobulinemia to reduce the likelihood of infection [4]. The development of PRCA or hypogammaglobulinemia was seen in 2 cases, which highlights the need for careful monitoring of the onset of these pathologies, as with myasthenia gravis, after surgery.

Although a standard treatment has not been established, extended thymectomy, immunosuppressive therapy, and intravenous immunoglobulin infusion may be performed in patients with PRCA associated with Good syndrome.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

