Multiple Sclerosis Following Splenectomy as a Treatment for Idiopathic Thrombocytopenic Purpura

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Abstract

A 27-year-old woman was admitted to our hospital with tetraparesis, dysesthesia and hypoesthesia of all regions below the breasts, urinary disturbance, and difficulty in breathing. Since age 21 idiopathic thrombocytopenic purpura (ITP) was diagnosed and steroid therapy was continued. At age 26, she had splenectomy for her ITP. On admission, steroid pulse therapy was administered with a tentative diagnosis of transverse myelitis. Symptoms gradually ameliorated. At age 29, she gradually lost her left vision, and multiple sclerosis was diagnosed and steroid therapy was administered, and her left vision gradually ameliorated. There are several reports describing other autoimmune disorders that arise after splenectomy. Since the spleen acts as a major pool of type 2 helper T cells, it is plausible that peripheral type 1 helper T cell activity may increase after splenectomy, promoting the development of autoimmune disorders. We considered there would be a close relation between splenectomy for ITP and multiple sclerosis in this case.

Key words: multiple sclerosis, idiopathic thrombocytopenic purpura, splenectomy, autoimmune disorders, T cell

Case Report

A 27-year-old woman was admitted to our hospital in October 2002 with tetraparesis, dysesthesia and hypoesthesia of all regions below the breasts, urinary disturbance, and difficulty in breathing. Since age 21, she had been diagnosed with ITP and steroid therapy had been continued. The diagnosis of ITP was based on leg purpurae, thrombocytopenia (platelet counts: 15,000/μl), polymegakaryocytethemia in bone marrow, high titers of platelet associated IgG (1,023 ng/10³) and exclusion of other diseases such as systemic lupus erythematosus. In 2001 (at age 26), she underwent successful splenectomy as therapy for ITP. On admission, magnetic resonance imaging (MRI) showed longitudinally scattered high signals on T2-weighted sequence from the medulla to the entire cervical cord. She was tentatively diagnosed as having transverse myelitis and steroid pulse therapy was performed; and symptoms gradually ameliorated.

In September 2004 (at age 29), she gradually lost her left vision and was readmitted to our hospital in October. On admission, general physical examination did not disclose any abnormalities. The patient did not have dry eye, mouth or any other sicca syndrome. Ophthalmologic examinations also did not disclose any abnormalities, but her left eye could only sense brightness. The corrected eyesight of the right eye was normal. On neurological examinations, the patient was awake and alert, and had no abnormalities in higher brain functions. There was no cranial nerve involvement other than that of the left optic nerve. Pupils were isocoric and light reflex was intact, but there was a relative afferent pupillary defect in the left eye. Muscles were not atrophic and did not demonstrate any weakness. Coordination was intact. Deep tendon reflexes were all symmetrical and moderately exaggerated. There were no pathological reflexes except for bilateral pathological plantar reflexes. The patient disclosed dysesthesia and hypoesthesia in all distal limbs, which remained as a persistent sequela. She had severe constipation, but other autonomic functions were intact.

Introduction

Splenectomy is sometimes performed to treat idiopathic thrombocytopenic purpura (ITP). There have been several reports describing other autoimmune disorders subsequent to splenectomy (1, 2). We described a case of multiple sclerosis that developed after splenectomy for ITP.
Blood analysis did not show any abnormalities other than mild thrombocytopenia (platelet counts: 65,000/µl) and a high index of the SS-A antibody (index: 91.1). Other antibodies such as antinuclear antibody, DNA antibody, SS-B antibody or RNP antibody were not detected. WBC and RBC were normal (WBC: 5,700/µl, RBC: 431×10^12/µl). Cerebrospinal fluid examinations showed high total protein (64.5 mg/dl) and mildly increased cell counts (7/mm^3). Oligoclonal bands and myelin basic protein were not detected. The IgG index was 1.13.

MRI showed high intensity signals of the swollen left optic nerve on short-tau inversion recovery (STIR) sequence. Furthermore, there were longitudinally scattered high signals on a T2-weighted sequence from the medulla to the entire cervical cord, and these signals had existed since the first attack (Fig. 1). There were no other abnormal lesions in the brain or spinal cord. Right visual evoked potentials were normal, but left visual evoked potentials could not be evoked.

The patient was diagnosed as having multiple sclerosis. Corticosteroid pulse therapy was performed and thereafter 40 mg/day prednisolone was prescribed orally. Oral prednisolone was gradually reduced and the left vision gradually ameliorated.

**Discussion**

We considered that there could be a close relationship between splenectomy for ITP and multiple sclerosis. Adults with ITP often have increased numbers of HLA-DR+ T cells and interleukin 2 receptors, and the cytokine profile suggests the activation of precursor helper T and type 1 helper T cells (3). In these patients, T cells stimulate the synthesis of antibodies after exposure to fragments of glycoprotein IIb/IIIa but not after exposure to native proteins (4). The derivation of these cryptic epitopes in vivo and the reason for the sustained T-cell activation are unknown.

Multiple sclerosis also shows a type 1 helper T cell-activation pattern. The pathologic features of multiple sclerosis reflect a type 1 helper T cell delayed hypersensitivity reaction, consistent with a cell-mediated immune process, as does the expression of interleukin 12 and type 1 chemokines in cerebrospinal fluid. Further, increased levels of gamma globulin and the presence of activated T cells in the cerebrospinal fluid demonstrate a localized immune response in the cerebrospinal fluid (5). However, it remains controversial whether multiple sclerosis is an autoimmune disease (6).

Splenectomy is followed by reduction of autoantibody peripheral blood titer (7, 8). Spleen cells isolated from ITP patients produce antiplatelet immunoglobulin in in vitro cultures (9). The percentage of T cells and B cells with activated phenotype is far greater in the spleen than in the peripheral blood of ITP patients (10). The number of circulating autoreactive anti-platelet T cells and B cells declines after splenectomy, leading to clinical remission. However, based on phenotypic studies showing the increased presence of T cells with an activated phenotype after splenectomy in ITP patients (11), it is plausible that peripheral type 1 helper T cell activity may increase after splenectomy.

Unfortunately we could not demonstrate cytokine data...
when the patient had splenectomy. After splenectomy, eosinophil was decreased 0.9% (65/µl) (just before splenectomy) to 0.1% (13/µl) (one day after splenectomy), when the patient was prescribed 50 mg oral prednisolone. This might mean loss of type 2 helper T cell activity.

There are several reports that have described the development of other autoimmune disorders following splenectomy (1, 2). Type 2 helper T cells are of importance in the maintenance of normal immunologic response, and the loss of type 2 helper T cell activity has been associated with the pathogenesis of autoimmune disorders (12). Since the spleen acts as a major pool of type 2 helper T cells, one might expect that splenectomy could evoke autoimmune phenomena, such as multiple sclerosis (13, 14). However, there are no cases reported with multiple sclerosis development or deterioration following splenectomy; this is the first presentation of multiple sclerosis developed after splenectomy.

Another possible explanation for this case is that some other disease, such as systemic lupus erythematosus or Sjögren’s syndrome, might be latent but could possibly cause ITP-like and multiple sclerosis-like changes. Although the patient did not fulfill the diagnostic criteria for systemic lupus erythematosus or Sjögren’s syndrome, careful follow-up remains necessary even though 9 years have passed.

References