Hypogammaglobulinemia 31 Years after the Diagnosis of Systemic Lupus Erythematosus

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The association of immunodeficiencies and autoimmunity is well established in the literature [1]. We report the case of a patient who developed hypogammaglobulinemia 31 years after being diagnosed with lupus, which is a rare intercurrence of this disease. We discuss the possible pathogenetic role of hypogammaglobulinemia and lupus.

Patient Description

A 58 year old woman of Iranian origin presented with recurrent prolonged sinus infections of 24 months duration. She was diagnosed with SLE in 1971 after the development of a malar rash, arthritis, serositis, positive antinuclear antibodies and positive anti-dsDNA antibodies. During the last 2 years the patient presented with recurrent sino-pulmonary infections despite appropriate antibiotic therapy and functional endoscopic sinus surgery, with clinical and laboratory quiescence of SLE. Serum examination revealed the existence of hypogammaglobulinemia (immunoglobulin M 0.4 g/L, IgG 2.81 g/L, IgA 1.27 g/L; reference intervals were IgM 0.53–3.34 g/L, IgG 6.14–12.95 g/L, IgA 0.6–3.09 g/L). One month later, she developed fulminant pneumonia but recovered following treatment with wide-spectrum antibiotics.

Comment

The apparently paradoxical association between hypogammaglobulinemia and autoimmunity is not fully understood. It is well established that patients with immunodeficiencies, particularly humoral, show an increased prevalence of autoimmune diseases in comparison to the general population [1].

Goldstein et al. [2] were the first to report on the development of common variable immunodeficiency and SLE, and six cases have been reported [2]. However, many authors suggest that this association might be underdiagnosed [3]. CVID is a heterogeneous group of hypogammaglobulinemias related to somatic aberrations of B cells, in contrast to X-linked hypogammaglobulinemia (Bruton's immunodeficiency), which is an inherited form of B cell deficiency. The most common hypogammaglobulinemia is the selective deficiency of IgA, which is believed to occur in as many as 1 to 600 individuals in the general population, and autoimmunity is the most prevalent disorder in this group of patients. It has been suggested that selective deficiency of IgA is a form of CVID, since it also represents a somatic aberration of B cells [1].

The accepted explanation for the association of hypogammaglobulinemia and autoimmune diseases is the hyperinflammatory state that is generated by recurrent infections due to activation of the innate immunity, namely complement system and toll-like receptors, which would then modify the physiologic immune reactivity by yet unknown means [1]. The role of immunomodulatory and immunosuppressive therapy in the induction of hypogammaglobulinemia has also been suggested [2] since the aim of therapy with these agents is the depletion of lymphocyte populations. However, other factors must be involved in the pathophysiology of the hypogammaglobulinemia in patients receiving this kind of therapy.

In addition, the key role of the idiotypic network in the immune physiology is to be considered. Since antibodies bind antibodies that bind antibodies [4], their mutual interactions would be required for the maintained self-regulation of the immune system. Hence, the hypogammaglobulinemia would represent the loosening of regulatory circuits of the immunologic network favoring the expansion of lymphocyte populations that change the healthy state of the immune system into a pathogenic one. As recently discussed by Stewart and Coutinho [5], the autoimmune phenomena would arise from the deficiency of these self-regulatory mechanisms, indicating a more rational link between immunodeficiency and autoimmunity.

In recent years the immunoglobulins and B cells have gained a special importance in our understanding of the immune system and the pathogenesis of autoimmune diseases. The association of hypogammaglobulinemia and autoimmunity might provide clinical insight into the role of antibodies in the immunologic physiopathology.

SLE = systemic lupus erythematosus
Ig = immunoglobulin

CVID = common variable immunodeficiency

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