

Common variable immunodeficiency

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ABSTRACT

We describe a patient with common variable immunodeficiency who three times presented an anaphylactic reaction after intravenous immunoglobulin administration. These reactions were attributed to the total absence of IgG 2, 3 and 4.

Key words: Common Variable Immunodeficiency. Congenital immunodeficiency. Anaphylaxis. Gamma-globulin administration.

RESUMEN

Paciente con inmunodeficiencia variable común que presentó en tres ocasiones una reacción anafiláctica tras la administración intravenosa de inmunoglobulina; este hecho se atribuyó a la ausencia total de IgG 2, 3 y 4.

Palabras clave: Inmunodeficiencia variable común. Inmunodeficiencia congénita. Anafilaxia. Administración de gammaglobulina.

INTRODUCTION

The Common Variable Immunodeficiency is a congenital immunodeficiency of the humoral immune system.

The principal hypothesis about the pathogeny of Common Variable Immunodeficiency is the loss of final capacity of Bursa equivalent lymphocytes differentiation to plasmacytes. There is a reduction of immunoglobulins whilst the number of B lymphocytes is almost always normal. Proliferation of B lymphocytes in the peripheral lymphoid organs is responsible for adeno and splenomegaly that can appear in these patients.

Among the differential diagnoses of Common Variable Immunodeficiency we have: Congenital Agammaglobulinemia, Infant Transitory Hypogammaglobulinemia, Hyper IgM Syndrome, IgG Subclass Deficiencies¹ and other diseases that cause recurring pneumonias.

There are three types of Congenital Agammaglobulinemia: Bruton's, Recessive Autosomal and, more rarely, Sporadic. Bruton's Agammaglobulinemia consists of an inherited defect linked to the X chromosome, with a higher prevalence in males. It is characterized by the absence of serum immunoglobulins and the reduction or absence of Bursa equivalent lymphocytes (B). In Bruton's disease, the gene that codes the Btk tyrosine kinase protein is defective, resulting in the interruption of B lymphocyte maturation in the pre-B-cell phase and decrease of B lymphocytes^{2,3,4}. The count of B lymphocytes is reduced or close to normal in recessive autosomal agammaglobulinemia. The altered genes code other maturation proteins, but not Btk.

Patients with Common Variable Immunodeficiency and Congenital

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Agammaglobulinemia usually present serious and repetitive episodes of pneumonia, due to IgG deficiency.

Treatment of Common Variable Immunodeficiency and Congenital Agammaglobulinemia consists of intravenous immunoglobulin administration^{5,6} in cases of deficiency of IgG classes or subclasses in patients that present recurring pneumonias⁷.

CASE REPORT

CR, seventeen-year-old female, was born in and is resident of São Paulo, Brazil. Reported having, since the age of three, recurring sinusitis and pneumonias (around six episodes a year). At the age of five was referred for immunological follow-up. She reported the need for antibiotic therapy and hospital admission during episodes of pneumonias, that became increasingly frequent and serious.

Familial immunodeficiency history was not discovered. In the physical exam she presented signs of malnutrition, hypo coloration of the mucous, cervical adenopathy, hypertrophic amygdalae, not hyperemic, free lungs, normal cardiac sounds, globose abdomen, palpable spleen five centimeters from left rib border, extremities and nervous system without apparent alterations. Laboratory exams showed IgA < 7 mg/dl, IgM = 18 mg/dl, IgG = 118 mg/dl, being IgG1 = 118 mg/dl and IgG 2, 3 e 4 absent, normal values of T and B lymphocytes, CD4 +, CD8 +, neutrophil and monocyte phagocytosis and chemotaxis. Similar values were maintained in the subsequent exams.

The patient diagnosed with Common Variable Immunodeficiency and intravenous gammaglobulin was administered. In the three attempts, the patient presented nausea, vomiting, swelling of the lips, cyanosis, swelling of the glottis, severe bronchospasm and low blood pressure. Gammaglobulin treatment was immediately suspended and the patient was treated for anaphylactic shock.

Because of the impossibility of intravenous immunoglobulin administration and the serious cases of pneumonia, prophylactic antibiotic therapy was established, with improvement of infection control.

DISCUSSION

Diagnosis of Common Variable Immunodeficiency was based on the clinical aspects of recurring sinusitis and pneumonia, with exams showing concentrations of IgA < 7 mg/dl, IgG < 200 mg/dl, IgM < 70 mg/dl and normal B-lymphocyte values.

The beginning of sinusitis progressing to recurrent episodes of pneumonia helps diagnosis of Common Variable Immunodeficiency that can be preceded for IgA deficiency, responsible for sinus pathology and for IgG subclass deficiency, characterized by repetitive pneumonia⁸.

The patient would require intravenous immunoglobulin infusion due to IgG deficiency and the repetitive episodes of pneumonia. This was attempted three times.

The first evolution to anaphylactic shock was interpreted as the presence of antibodies against that particular immunoglobulin lot. Because of the recurrence of anaphylactic shock with the other two intravenous gammaglobulin lots and because of the dosage of the IgG subclasses the main suspicion was reaction to the IgG 2, 3 e 4, because the patient present total absence of the same. This hypothesis was made in analogy to IgA deficiency, where the patient doesn't present any trace of serum IgA and it is possible to evolve to anaphylactic reaction because of anti-IgA antibody formation⁹⁻¹³.

It is known that in the beginning of life there is a negative clonal selection in the central organs induced by a high affinity between endogenous peptides and the TCR of T lymphocytes. The second negative clonal selection in the central organs occurs because of the high affinity between MHC I antigen-presenting cells to CD8 + and MHC II and CD4 +. The negative clonal selection causes the elimination of auto-reactive cell-clones. After this selection, lymphocytes retain the capacity to react against substances considered foreign to the organism. For our patient, IgG 2, 3 and 4 are considered foreign substances to her immune system. Negative clonal selection probably did not occur for these immunoglobulins and subjected to them, these being glycoproteins of 96 % polypeptidic of and 4 % carbohydrate composition making them strongly antigenic could cause anaphylaxis. This would be the same process that occurs in patients with total IgA absence, because of anti-IgA antibody formation^{14,15}, needing depleted IgA gammaglobulin^{16,17}.

We conclude that the exhibited anaphylaxis could be due to a total absence of IgG 2, 3 e 4, especially because laboratory gammaglobulin is rich in these immunoglobulin isotypes.

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