

Section: CLINICAL CASE REPORT

Abstract: CCR-05

The broad spectrum of immune dysregulation: clinical cases

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INTRODUCTION: Inborn errors of immunity are classified according to the many possible genetic defects, and 25% manifest as immune dysregulation. CTLA-4 (cytotoxic T-lymphocyte antigen 4) haploinsufficiency has been associated with variable clinical presentations, ranging from asymptomatic carriers (30%) to patients with severe disease that may result in death. CTLA-4 is an inhibitory coreceptor found on immune-cell membranes, particularly on activated T cells and regulatory T cells (Tregs). Symptoms are related to autoimmunity and inflammation, as well as infectious processes caused by hypogammaglobulinemia. The authors describe two patients with CTLA-4 haploinsufficiency and different clinical manifestations. **CASE REPORTS:** Case 1 was a 9-year-old boy born to healthy parents. From early childhood, he had poor weight and height gain and developed microcytic anemia at nine months of age. At five years, he was diagnosed with Evans syndrome, with fever, petechiae, bruising, and jaundice. Immunoglobulin replacement and corticosteroid treatment were then initiated. He had several subsequent hospitalizations for severe diarrhea resulting in dehydration and electrolyte disturbances. Because the condition persisted, genetic sequencing was performed (c.443A>C: p.Q148>P), and abatacept was initiated based on the result. The patient did not improve and continued to experience infections. Hematopoietic cell transplantation was indicated; complications occurred, and the patient died. Case 2 was a 9-year-old boy with a healthy mother and a father previously diagnosed with Hodgkin lymphoma (the father did not undergo genetic testing). At five years, the patient developed autoimmune hemolytic anemia and hypogammaglobulinemia. A genetic panel was requested because of his clinical history and identified a pathogenic variant (c.380A>G: p.Tyr127>Cys). At six years, he was hospitalized for thrombocytopenia (2,000/mm³), after which abatacept and immunoglobulin replacement were initiated, with normalization of the platelet count. He remains on treatment and clinically stable. **DISCUSSION:** These two cases of CTLA-4 haploinsufficiency had distinct clinical manifestations and severity. Both combined symptoms of autoimmunity and immunodeficiency that began in early childhood, but their courses differed. The main target organ in the first case was the intestine, whereas the hematopoietic system predominated in the second. Both patients had severe manifestations such as cytopenias and enteropathy, but the second patient responded favorably to treatment.

KEYWORDS: Immune dysregulation; Innate immunity; CTLA-4.