strategies, such as positive stem cell selection and double autotransplant, to improve CR rate in this subgroup of patients.

Key words

Autologous stem cell transplantation, multiple myeloma

Correspondence

Dr. Francesca Patriarca, Division of Hematology, Udine University Hospital, p.le S. Maria della Misericordia, 33100 Udine, Italy. Phone international +39-432-559662 • Fax international +39-432-559661.

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Enzyme replacement therapy decreases hypergammaglobulinemia in Gaucher's disease

Joëlle Deibener,* Pierre Kaminsky,* Christine Jacob,° Brigitte Dousset,° Marc Klein,* Michel Duc*

**Department of Internal Medicine; °Laboratory of Biochemistry, Centre Hospitalier Universitaire de Nancy, France*

We report the effects of enzyme replacement therapy in a patient with Gaucher's disease associated with a monoclonal gammopathy. Alglucerase induces a linear decline in immunoglobulin and β_2-microglobulin levels. This observation suggests that this treatment decreases the chronic antigenic stimulation commonly found in Gaucher's disease.

Gaucher's disease (GD) is characterized by genetic deficiency of lysosomal glucocerebrosidase. The subsequent accumulation of glycosylceramide in macrophages results in enlargement of the spleen and liver, bone marrow infiltration, and hematological disorders[1] and has been in part linked to the overload reticuloendothelial system.[2] A chronic B-cell stimulation, expressed by the development of hypergammaglobulinemia, has been documented in GD. We report the effects of enzyme replacement therapy on immunoglobulin abnormalities in a patient with type-I Gaucher's disease associated with hypergammaglobulinemia.

A 39-year-old man presented with a long history of GD with marked pancytopenia, hepatomegaly, splenomegaly, bilateral femoral head osteonecrosis and bone deformities. An M-component of IgGκ type (28 g/L). and three other smaller clones, respectively of IgG-κ, IgG-λ and IgA-λ type, were demonstrated by immunofixation electrophoresis. Serum IgA and IgM levels were respectively 1.45 g/L and 1.04 g/L. Low levels of Bence-Jones protein were found in urine (50 mg/L) and elevated β_2-microglobulin at 6.2 mg/L in serum (normal < 2.4 mg/L). No plasma cell proliferation was observed in bone marrow aspirate by immunofluorescence study. Extensive radiological investigations ruled out multiple myeloma or lymphoma.

Alglucerase (Ceredase®, Genzyme Co, Cambridge, MA, USA), administered at 60 IU/kg every two weeks, induced a linear decline in β_2-microglobulin level, which reached a quasi-normal value after 2 years (Figure 1). A parallel fall in IgA and IgM immunoglobulins, and a significant decline in the monoclonal IgG-κ paraprotein were observed (Figure 2). At immunofixation electrophoresis, the three smaller monoclonal gammopathies progressively disappeared. Moreover, Bence-Jones proteinuria vanished.

Polyclonal, oligoclonal or monoclonal hypergammaglobulinemia has been reported in GD.[2-4] In addition to marked splenomegaly or hepatomegaly, aseptic necrosis, chronic infections, liver diseases, decreased antigen clearance secondary to an overload reticuloendothelial system, excessive chronic antigenic stimulation secondary to distorted lipid metabolism, or defects in immunoregulation of B-cell function have been also implicated in the pathogenesis of the immune disorders.[3] Glucocerebroside has been found to activate immunoglobulin production by non-specifically stimulating macrophage interleukin-1 secretion.[5] As observed in our patient, the decline in β_2-microglobulin and gammaglobulins during alglucerase treatment suggests that enzyme replacement therapy may reduce the antigenic stimulation, either by restoring the macrophage ability to hydrolyze the glycosylceramide, leading to decrease macrophage stimulation, or by decreasing the amount of accumulated glycerylceramide. Reduction in hypergammaglobulinemia and in serum M-component level after splenectomy have been previously reported.[4, 6-8]

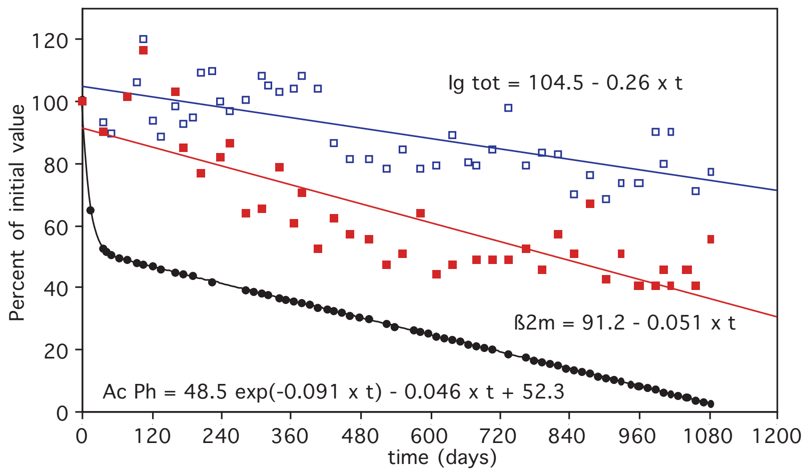

Figure 1. Comparison of the time-course of total immunoglobulin (Ig tot), β_2-microglobulin (β_2M) and acid phosphatase (Alc Ph) levels during enzyme replacement therapy, after normalizing of initial value to 100%.

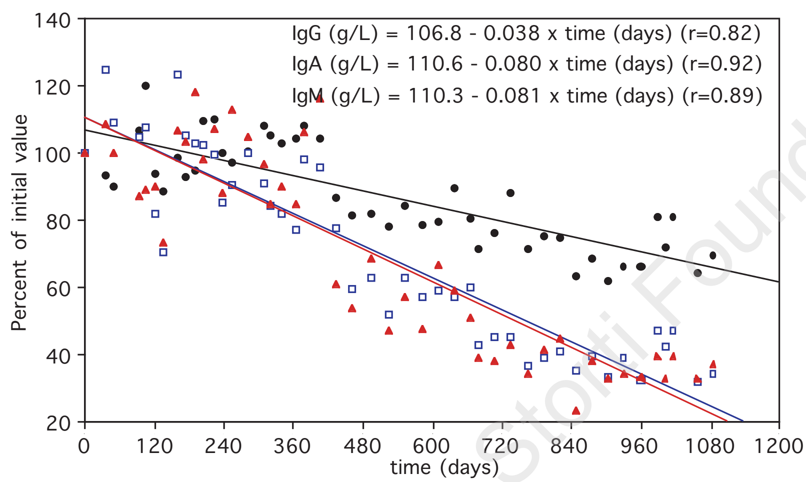

Figure 2. Time evolution of IgG (filled circles), IgA (open squares), and IgM (filled triangles) levels during alglucerase treatment, after normalizing of initial value to 100%.

Chronic immune disorders in GD might induce B-cell neoplasm.[9,10] One can therefore postulate that the treatment could contribute to decrease the risk of hematopoietic cancers. This hypothesis needs further investigations, but is worth evaluating when taking into account the cost of the treatment. Moreover, β_2-microglobulin level as a marker for the follow-up of patients with GD requires further studies.

Key-words

Gaucher's disease, hypergammaglobulinemia, β_2-microglobulin

Correspondence

Joëlle Deibener, MD, Service de Médecine Interne, CHU de Nancy, Hôpitaux de Brabois, 54500 Vandoeuvre, France. Phone international +33.3.83154060 • Fax international +33.3.83153826.

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