Efficacy of GH treatment in a patient with chronic granulomatous disease, who developed acute myeloid leukemia after bone marrow transplantation

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Chronic granulomatous disease (CGD) is a rare primary immunodeficiency. Growth retardation is a common finding, due to recurrent severe infections and inflammatory complications. Bone marrow transplantation (BMT) can lead to stable remission, with overall pediatric survival rates >90% after non-myeloablative conditioning transplants. As reported in previous studies, growth rates in CGD recovered following BMT.

At the age of 8 years, an Egyptian boy affected by CGD, underwent BMT from his healthy HLA identical sister. Previous medical history included recurrent lymphadenitis, osteomyelitis and pulmonary aspergilloma. At that time, his height was -1.51 SDS (according to WHO growth charts), appropriate for target height (-0.68 SDS). A diagnosis of acute myeloid leukemia (AML) was made two years later. He was treated according to AIEOP (Italian Association of Pediatric Hematology and Oncology) AML 2002 protocol and reached complete remission after a second BMT. After one year, he developed chronic hepatic graft versus host disease (GVHD). At the age of 12, in the absence of minimal residual disease in the last 2 years, a deceleration in growth velocity (height -1.85 SDS, growth velocity -1.9 SDS) was found and growth hormone deficiency (GHD) was diagnosed (first test peak 7.9 ng/ml, second test peak 1.9 ng/ml, IGF-1 below the normal range, 2-year delayed bone age, Tanner stage 1). Brain MRI performed before treatment was normal. GH replacement therapy was started at a dosage of 31 mcg/kg/day, with initial growth improvement. Eight months later the treatment was suspended for AML relapse with central nervous system involvement. The boy underwent a third BMT, this time from a matched unrelated donor, with a subsequent stable disease remission. At 14 years, in the absence of minimal residual disease, considering a persistent growth impairment (height -2.64 SDS, growth velocity -5.67 SDS, Tanner stage 1), IGF-1 low levels and 2-year delayed bone age, he resumed treatment with somatropin at a dosage of 15 mcg/kg/day. Growth rate improved (8.86 cm/year, +4.48 SDS), according to a good spontaneous pubertal progression. At the age of 18, his final height was 165 cm (-1.47 SDS), appropriate for target height. Since GH effects are partly mediated through IGF-I, which after generation in the liver can act via the endocrine pathway, in this case, despite chronic GVH of the liver, IGF-1 levels never turned into pathological levels during GH replacement therapy.

We present a complex case of CGD who developed AML after transplantation. Main growth impairment became evident after AML onset. Despite two leukemic relapses and chronic GVHD associated with negative influences of multiple chemotherapies and pre-transplantation conditioning (but without body irradiation), standard dosage of GH was effective in improving growth and final height.

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References