Our patient was a 7-year-old Italian boy born after an uneventful gestation of normal duration.
At the age of 16 months, he presented with a clinically evident enlarged abdomen and was referred for oncological examination.
Initial tests revealed anemia, thrombocytopenia, and splenomegaly.
A bone marrow biopsy revealed the presence of foam cells, which led to suspicion of lysosomal storage disease.
Biochemical testing revealed elevated level of acid phosphatase (47.8 IU/L [normal range 5–7 IU/L]) and chitotriosidase activity (508 nmol/mg protein [normal range 5.9–41.0 nmol/mg protein]), as well as reduced beta-glucosidase activity (2 nmol/mg/protein [normal range 4.5–18.0 nmol/mg/protein]).
Molecular analysis showed homozygous L444P mutations in the GBA gene (OMIM reference 606463), confirming the diagnosis of chronic NGD.
The patient began ERT at a dosage of 60 U/kg every 2 weeks at the age of 18 months.
Thereafter, when the patient reached the age of 30 months, we decided to combine ERT with SRT with miglustat.
This clinical decision was approved by our institution's ethics committee, and informed consent was obtained from the patient's parents before commencing combination therapy.
The dose of miglustat was adjusted according to the patient's body surface area and was uptitrated during the first 4 weeks with the following scheme: one-third of target dose during weeks 1 and 2, two-thirds of target dose during weeks 3 and 4, and target dose (100 mg three times daily) after 1 month.
From 2 weeks before starting miglustat therapy, the patient also followed specific dietary modifications, avoiding high intake of carbohydrate-containing food in single meals, especially foods high in disaccharides, such as sucrose and maltose, to ensure acceptable gastrointestinal tolerability.
He experienced mild episodes of diarrhea after commencing miglustat therapy, which decreased in frequency/severity over time.
From the start of ERT/miglustat combination treatment, we observed a reduction in splenomegaly and a gradual normalization of hematological values and plasma angiotensin-converting enzyme activity (Table 1).
Plasma chitotriosidase was evaluated at the time of diagnosis and then approximately every 6 months during follow-up.
Values showed an initial reduction after the start of ERT, with a further, substantial, and sustained decrease after commencement of miglustat treatment (Fig.1).
The patient has been followed according to recommended guidelines for GD, which specify a complete neurological examination, clinical evaluation of ocular movements, and psychological evaluations every 6–12 months [10].
After 5 years of combination therapy and follow-up, the patient did not show any signs of neurological impairment.
As of February 2016, he had not displayed any epileptic crises and had demonstrated clinical performance and cooperation.
He showed good muscular tone and trophism, normal reflexes with a slight hyperreflexia in his legs, and a negative Romberg sign.
His toe and heel deambulation was normal.
In particular, ocular evaluations revealed no evidence of saccadic movement velocity reduction and normal visual evoked potentials.
The patient's auditory brain responses were also normal.
In addition, he has not demonstrated any cognitive impairment, and he has regularly attended school with good performance since the age of 5 years.