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SHORT REPORT

Treatment of Niemann–Pick disease type C in two children with miglustat: Initial responses and maintenance of effects over 1 year

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Summary Niemann–Pick disease type C (NP-C) is a lipid storage disorder characterized by the accumulation of unesterified cholesterol and glycolipids in the lysosomal/late endosomal system of certain cells in the central nervous system (CNS) and visceral organs. Clinical symptoms include progressive neurological deterioration and visceral organomegaly. Miglustat, a small iminosugar molecule approved for the treatment of Gaucher disease, reversibly inhibits glucosylceramide synthase, which catalyses the first committed step in glycosphingolipid synthesis. The physicochemical properties of miglustat allow it to cross the blood–brain barrier and suggest possible benefits in lysosomal storage diseases affecting the CNS. Here, we present findings in two children with NP-C, aged 14 years (patient 1) and 9 years (patient 2), treated with miglustat for 1 year. Before treatment, patient 1 presented with severe difficulties in swallowing and walking, and patient 2 with problems mostly affecting communication and social interaction. Videofluoroscopic studies in patient 1 demonstrated a substantial improvement in swallowing by month 6 of treatment, and ambulation index measurements indicated improved walking. Mini Mental-State Examination (MMSE) assessments in patient 2 showed cognitive improvement by month 6, which was sustained up to month 12. Liver/spleen volume and plasma chitotriosidase activities were stabilized in both cases. There was no weight loss during treatment. Patient 1 experienced severe but self-limiting paresthesia, which was not associated with peripheral neuropathy. We conclude that miglustat can provide therapeutic benefits in CNS symptoms and allows stabilization of systemic disease in childhood-onset NP-C. Further follow-up is crucial to determine the long-term maintenance of these effects.

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Electronic Supplementary Material
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