Two Unexpected Manifestations in the Diagnosis and Follow-up of Gaucher Disease Type 3

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Background

In Gaucher disease (GD), the accumulation of glycosylceramide/glucocerebrosride and some related compounds primarily results in cytopenia, hepatosplenomegaly and bone manifestations. Other accompanying findings have also been described such as hepatic fibrosis and pulmonary hypertension in GD type 1; congenital ichthyosis in GD type 2; corneal opacity, cardiac and vascular calcifications in GD type 3. Delayed puberty was shown in 60% of GD type 1 patients. However, congenital ichthyosis as well as precocious puberty have never been described in GD type 3.
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Case presentation

A 10 months-old male patient presented with ichthyosis, failure to thrive and hepatosplenomegaly. He had a family history of isolated ichthyosis. Laboratory analysis showed mild anemia and thrombocytopenia as well as high chitotriosidase (3359 nmol/hour/ml) and low glucocerebrosidase levels [1.84 nmol/hour/mg protein (9.4±3.2)]. Radiological assessment revealed that liver and spleen were 2.5 and 22 times the upper normal limits (UNL), respectively. A homozygous mutation of L444P in GBA gene confirmed the diagnosis of GD.

Morphological findings in skin biopsy supported X-linked or lamellar ichthyosis. No bone manifestations were determined. Due to good neurologic status at the time of diagnosis, the patient was not classified as GD type 2. Imiglucerase treatment (60 U/kg) was started immediately. Significant hematologic and visceral improvement was observed by the first year of treatment. By the 3rd age, the patient achieved normal growth rate, but lateral downward gaze palsy, mild developmental delay and convulsions occurred so that the patient was classified as GD type 3. The neurological symptoms did not worsen by time and seizures were controlled by antiepileptic drugs.

At the age of 8.5, in addition to mild splenomegaly (radiologically spleen=4.4xUNL), pubic hair development (stage 2) with increased testicular volume (left 10 ml, right 12-15 ml) were realized. Central precocious puberty was diagnosed with the findings of advanced bone age (10 years old) and high LH level (LH:1.96 IU/L). Magnetic resonance imaging of brain and hypophysis excluded intracranial tumors and lesions.
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Discussion

In this poster presentation, we present a patient with GD because of two interesting findings, one causing diagnostic confusion and the other unexpected. Ichthyosis along with neurological manifestations has been reported in acute neuronopathic form (GD type 2) and is associated with early-onset death. It has never been reported in patients with GD type 1 or 3. The family history of ichthyosis and relatively mild clinical course of our patient has directed us to rule out GD type 2. Hence, ichthyosis was accepted as an incidental finding.

Delayed puberty is associated with a late diagnosis of GD type 1. Precocious puberty has not been reported related to GD and could be incidental. However, our experience showed that pubertal development in GD patients should be monitored as part of every visit not only to monitor for delayed puberty but also for timely diagnosis of early-onset puberty in younger patients.