CASE REPORT

Patient with Niemann-Pick disease type C: over 20 years' follow-up

Kazuo Abe,†Norio Sakai‡

SUMMARY

We report a 37-year-old woman with Niemann-Pick disease type C (NPC) 1. At the age of 8 years, she presented slow running followed by both fingers dystonia at the age of 10 years. At the age of 16 years, she developed declined scholastic achievement. On her first visit at the age of 17 years, she showed dystonia, ataxic gait and vertical supranuclear gaze palsy. We suspected it was NPC. She presented atrophies in the frontal lobes, brainstem and cerebellum in a brain MRI. She presented hepatomegalias and splenomegalias in an abdominal CT. At the age of 26 years, she undertook perpetually tracheal fistula because of recurrent aspiration pneumonia. Diagnosis of NPC1 was made by filipin staining and existence of foamy cells in the bone marrow and NPC1 gene analysis. We obtained informed consent of genetic analysis. Miglustat therapy was started at the age of 32 years. Improvements in swallowing capacity and in muscle tonus were seen.

BACKGROUND

Niemann-Pick disease type C (NPC) is an autosomal recessive neurovisceral lysosomal storage disorder resulting from mutations of either the NPC1 or the NPC2 gene, showing a wide spectrum of clinical phenotypes and a highly variable age at diagnosis, and most patients have normal routine examinations (MRI, cerebrospinal fluid, electrophysiology and so on).1–5 Thus, its diagnosis is often a challenge, delaying the start of treatment for several years.

We report a 37-year-old woman with NPC1 whom we continuously follow for over 20 years.

CASE PRESENTATION

Patient is a 37-year-old woman. At the age of 8 years, she presented slow running followed by both fingers dystonia at the age of 10 years. At the age of 16 years, she developed declined scholastic achievement.

On her first visit at the age of 17 years, she showed dystonia in all limbs, dysarthria, ataxic gait and vertical supranuclear gaze palsy (VSGP). On neurological examinations, she had VSGP without horizontal gaze palsy and abnormal coordination predominantly in lower limbs but had normal cranial nerve function and normal muscle strength. She had normal autonomic functions. Because of VSGP and dystonia, we suspected it was NPC. She presented atrophies in the frontal lobes, brainstem and cerebellum in a brain MRI (figure 1). She presented hepatomegalias and splenomegalias in an abdominal CT (figure 2).

Following MRIs showed developing atrophies in the brain and diffuse T2 high signals in the white matter. Electroencephalographic (EEG) matched criteria for diffuse generalised encephalopathy. Her gait disturbances due to dystonia and cerebellar ataxia gradually developed but could walk without assist until the age of 21 years. Her VSGP and dystonia gradually developed, and her horizontal eye movements was normal. She experienced frequent falls, and she eventually used wheel chair at the age of 22 years. She gradually developed difficulty in swallowing, and a percutaneous endoscopic gastrostomy was initiated. At the age of 26 years, she undertook perpetually tracheal fistula because of recurrent aspiration pneumonia. She could communicate with her facial expression when she was asked.

DIFFERENTIAL DIAGNOSIS

NPC is characterised by heterogeneous and oligosymptomatic presentation of visceral, neurological and psychiatric manifestations, making for difficult and often delayed diagnosis. Diagnosis of NP-C is made via physical assessment of the patient, biochemical tests involving filipin staining of skin fibroblasts and genetic sequencing of the NPC1 and NPC2 mutations. For physicians unfamiliar with NPC, at this time, the NPC Suspicion Index screening tool was developed by an international panel of NPC clinical experts.

TREATMENT

Miglustat was first approved for treatment of progressive neurological deterioration in children and adults with NPC based on preclinical evidence, a randomised controlled trial, long-term extension studies and a retrospective cohort study.

OUTCOME AND FOLLOW-UP

Diagnosis of NPC1 was made by filipin staining (figure 3A) and existence of foamy cells (figure 3B) in the bone marrow, and NPC1 gene analysis: c.2186 G>A (p.G729E), c.2374-2A>G. We obtained informed consent of genetic analysis. Miglustat therapy was started at the age of 32 years. Improvements in swallowing capacity and in muscle tonus were observed. She developed constipation, but no other adverse reactions were observed for 4 years after prescription of miglustat.
for minutes. She had vertical supranuclear gaze palsy without horizontal gaze palsy and abnormal coordination predominantly in lower limbs but had normal cranial nerve function and normal muscle strength. She can express her will by facial expression and by preserved horizontal eye movements.

**DISCUSSION**

Miglustat therapy improved swallowing capacity and muscle tonus. She developed constipation, but no other adverse reactions were observed for 4 years after prescription of miglustat. We believe that prescription of miglustat seems to be useful for improving and preserving her neurological signs and symptoms. Among the various neurological signs, VSGP and dystonia should be considered as highly important signs for juvenile/adult-onset NPC diagnosis. Because prescription of miglustat is helpful, early treatment in the disease course shows improved responses, highlighting the need for rapid diagnosis. In patients with atypical symptomology, a careful examination for VSGP is critical to enhance diagnostic accuracy in potential NPC.

**Learning points**

- Niemann-Pick disease type C (NPC) is a rare disease.
- Diagnosis of NPC is somewhat difficult.
- Miglustat may be effective.

**REFERENCES**


**Contributors**

KA: project development, data collection and manuscript writing. NS: critical review of the manuscript.

**Competing interests**

None declared.

**Patient consent**

Obtained from guardian.

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