

# Canavan disease: a rare form of leukodystrophy

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## Abstract

Canavan disease (CD) is a rare autosomal recessive leukodystrophy characterized by spongy degeneration of the white matter of brain. It is characterized by accumulation of N-acetyl aspartic (NAA) acid in mitochondria which inhibits myelin synthesis. Axial hypotonia, ataxia, defects in cognitive functions, defective visual follow and sucking, irritability and macrocephaly are seen in the patients. Increased high NAA peaks are seen magnetic resonance spectroscopy (MRS). Here we report a case with defective head control and could not sit without support who had no other symptoms before. She had axial hypotonia and bilateral nystagmus on neurological examination. The diagnosis of CD is based on these clinical findings and radiologic evaluations.

**Keywords:** Leukodystrophy; Canavan Disease; Magnetic Resonance Spectroscopy.

## INTRODUCTION

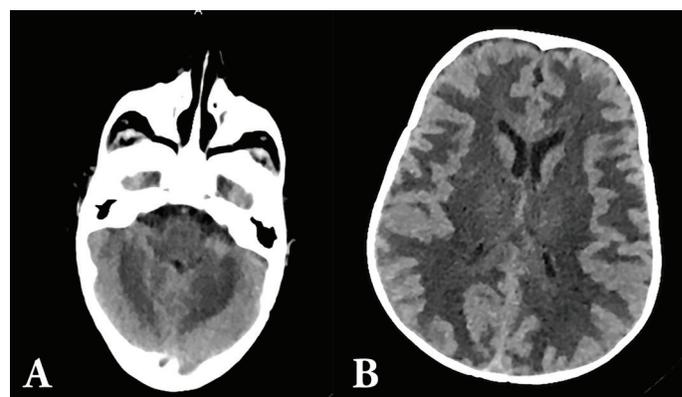
Canavan disease (CD) is a rare autosomal recessive leukodystrophy characterized by spongy degeneration of the whitematterofbrain. It is characterized by accumulation of NAA because of a defective aspartoacylase enzyme that cleaves N-acetyl group from NAA. Accumulation of NAA in mitochondria inhibits myelin synthesis (1). In the first months of the life axial hypotonia, ataxia, defects in cognitive functions, defective visual follow and sucking, irritability and macrocephaly are seen in these patients. They are lost before they reach to adolescence with optic atrophy and convulsions (2). Diagnosis is made with magnetic resonance imaging (MRI) that shows signal anomalies in basal ganglia and white matter including U fibers and with magnetic resonance spectroscopy (MRS) that shows increased NAA peak (3). Here we represent a case diagnosed as CD with these clinical findings and radiological evaluations.

## CASE REPORT

A seven month old girl, third child of a first degree relative mother and father, admitted to hospital for evaluation of neurological development who had defective head control and could not sit with or without support and had no other symptoms before. Other sisters of the child were healthy and she had a normal antenatal and perinatal period. She was macrocephalic (> 97%). Bilateral nystagmus was present in the eye movements of the patient with axillary hypotonia on neurological examination. Deep tendon

reflexes were increased. She had a 1-2 clap clonus and all other neurological findings of the patient were normal. No other pathology was detected in the other system examinations.

Brain computed tomography has a symmetrical widespread hypodense appearance in dentate nuclei, brain stem in infratentorial sections (Figure 1a), and whole white matter including periventricular area in supratentorial sections (Figure 1b).



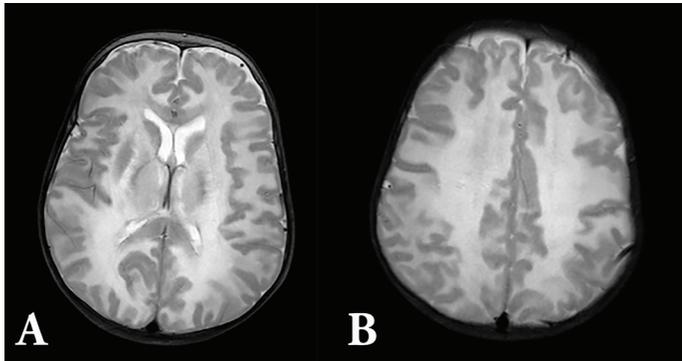
**Figure 1.** Brain CT, symmetric hypodense areas in (A) dentate nuclei and brain stem, (B) whole white matter including periventricular area

In brain MRI T2 sequence, diffuse hyperintense signal changes were observed in globus pallidus and bilateral

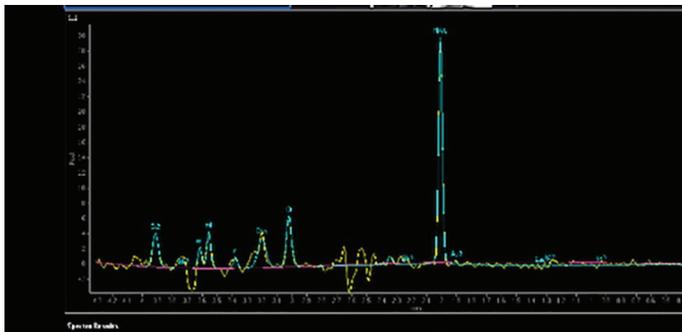
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thalamus, including U fibers in bilateral subcortical, periventricular deep white matter (Figure 2a, b). There were no signal changes in bilateral putamen and caudate nuclei. In the MRS assay centered at the level of centrum semiovale and periventricular white matter at TE 135 ms, there is a pronounced NAA peak (Figure 3).



**Figure 2.** Brain MRI T2A images show diffuse hyperintense signal changes in (A) bilaterally subcortical, periventricular deep white matter, globus pallidus including (U) fibers and (B) centrum semiovale



**Figure 3.** Marked NAA pike seen in MRA spectroscopy at TE 135 ms

## DISCUSSION

Canavan Disease is an autosomal recessive, serious, progressive form of a leucodystrophy. Can be seen in any ethnic group but mostly seen in Askenazi Jews. If the both parents are carrier for the disease, 25% of the children should be affected. Because of this, American obstetric and gynecology association suggested a screening genetic carrier test to all Askenazi Jewish parents in 1998 (4). We think it is important to notice that in our case, the parents of the child were first degree relatives.

Leukodystrophies are seen in the clinic with different findings. Usually CD is known to be diagnosed at 3-6 months, was diagnosed at 7 months in our patient. Although patients were reported to have irritability and swallowing difficulty, those findings were not detected in our patients. The hypotonia seen at the onset of the disease progresses into spasticity over time and the patients gain posture in the form of a flexion in the extremities. Our patient, who could not

sit without support and support, could not hold his head, was compatible with the initial stages of these findings. It has been reported that macrocephaly, which is present in the course of the disease and which also was present in our patient, is a typical finding. In CD, affects in cerebral and cerebellar subcortical white matter is observed to be severe, symmetrical and tendency to join. At the beginning, central white matter is preserved (5). Symmetrical involvement is seen in globus pallidus and thalamus, but not in putamen and caudate nuclei. The most characteristic finding is the involvement of subcortical U fibers (3). In our patient, MRI showed hyperintense signal changes in subcortical, periventricular deep white matter, U fibrils and globus pallidus (Figure 2). The MRS is requested from the patient because of the MRI findings that were consistent with the CD reported in the literature. Specific NAA pike in MRS was also detected in our patient which is specific for CD (Figure 3) (6).

Diffusion restriction at periventricular white matter, globus pallidus, thalamus, brain stem and dentate nuclei were reported as diffusion magnetic resonance imaging findings of CD (7,8). We could not studied diffusion MRI because the patient was referred to us from an other center.

In the literature, increased urinary NAA excretion was reported but urinary NAA level was not evaluated in our patient (9). Biochemical blood studies were normal. Although congenital, infantile and juvenile forms of canavan disease have been reported, infantile form is most commonly seen (10). Milder atypical forms are also reported, which are thought to be due to the variability of genetic component severity (11,12).

With these clinical and radiological findings, a leukodystrophy CD was considered in the patient and a mutation analysis with genetic screening was planned.

## REFERENCES

1. Matalon R. Aspartic acid (Canavan Disease) In: Kliegman, Behrman, Jenson, Stanton, eds. Nelson Textbook of Pediatrics. 18th edition. New Delhi: Elsevier. 2008. pp. 563-5.
2. Hoshino H, Kubota M. Canavan disease: clinical features and recent advances in research. *Pediatr Int* 2014;56(4):477-83.
3. Michel SJ, Given CA. Case 99: Canavan disease. *Radiology* 2006;241(1):310-4.
4. Kaul R, Gao GP, Balamurugan K, Matalon R. Canavan Disease: molecular basis of aspartoacylase deficiency. *J Inherit Metab Dis* 1994;17(3):295-7.
5. Van der Knaap MS, Valk J. Neuronal ceroid lipofuscinoses. In: *Magnetic resonance of myelination and myelin disorders*. 3rd. Berlin: Springer-Verlag 2005;326-33.
6. Wittsack HJ, Kugel H, Roth B, Heindel W. Quantitative measurements with localized <sup>1</sup>H MR spectroscopy in children with Canavan's disease. *J Magn Reson Imaging* 1996;6(6):889-93.
7. Sener RN. Canavan Disease: diffusion magnetic resonance imaging findings. *J Comput Assist Tomogr* 2003;27(1):30-3

8. Unlu HA, Altinbas NK, Teber S, Derinkuyu B, Unlu SE, Guleroglu NB, et al. Canavan disease MRI and MRS findings: 3 different cases. *Turkish Pediatr Dis* 2013;4:201-5.
9. Al-Dirbashi OY, Rashed MS, Al-Qahtani K, Al-Mokhadab MA, Kurdi W, Al-Sayed MA. Quantification of N-acetylaspartic acid in urine by LC-MS/MS for the diagnosis of Canavan disease. *J Inherit Metab Dis* 2007;30(4):612. Epub 2007 Jul 12.
10. Janson CG, Kolodny EH, Zeng BJ, Raghavan S, Pastores G, Torres P, et al. Mild-onset presentation of Canavan's disease associated with novel G212A point mutation in aspartoacylase gene. *Ann Neurol* 2006;59(2):428-31.
11. Yalcinkaya C, Benbir G, Salomons GS, Karaarslan E, Rolland MO, Jakobs C, et al. Atypical MRI findings in Canavan disease: a patient with a mild course. *Neuropediatrics* 2005;36(5):336-9.
12. Nguyen HV, Ishak GE. Canavan disease-unusual imaging features in a child with mild clinical presentation. *Pediatr Radiol* 2015;45(3):457-60.