TO THE EDITOR

Functional Neuroimaging Might Enable the Early Diagnosis of Neuroacanthocytosis

Neuroacanthocytosis (NA) syndromes refer to a group of genetically diverse conditions, complicated by basal ganglia degeneration, movement disorders, cognitive impairment, neuropsychiatric problems and misshapen red blood cells (acanthocytosis, deformed erythrocytes with spike-like protrusions).1,2 Currently available diagnostic criteria include peripheral blood smear, serum creatine kinase (CK) level, liver enzyme levels, neuromuscular tests and neuroimaging of caudate nucleus atrophy.1,2 Mutations in the VPS13A gene have been reportedly associated with NA disorders.3 However, due to the large gene size and various mutation sites, the confirmatory DNA analysis is only available in very few laboratories. There are no curative or disease-modifying treatments at present for NA patients1,2 but early diagnosis and timely treatment may improve the quality of their lives. Previous study demonstrated decreased FDG uptake in the basal ganglia of a NA case on the FDG-PET (positron emission tomography) images,4 but PET-CT (computed tomogram) is expensive and not widely available. Here, we report the single photon emission computed tomography-computed tomography (SPECT-CT) and magnetic resonance (MR) findings of a confirmed NA patient.

CASE REPORT

A 37-year-old man, a construction worker, was admitted to the Department of Neurology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (TMC&HUST). This patient had a history of orofacial involuntary movements, dysarthria, dysphagia, memory decline and gait abnormality for six months. The patient had no family history of involuntary movement disorders. His symptoms, which progressed gradually, were characteristically random, abrupt, irregular and involuntary, included occasional neck flexion, intermittent rapid brief eye closures, involuntary facial and neck movements, tongue- and lip-biting, and mimicked sucking and grimacing activities while making sucking sounds. The patients also suffered from executive functions impairment, poor attention, left lower extremity dystonia and gait abnormality. The prosody of the patient’s speech was irregular and slurred with a pronounced nasal quality. The distal muscles of his right upper extremity were atrophic and the muscular tension was diminished. Deep tendon reflexes and plantar responses were all absent. The relative clinical test of his liver, gallbladder, spleen, kidney, lungs and heart revealed no obvious abnormalities. A significant elevation in a serum CK (325, 38-174 U/L), l-lactate dehydrogenase (286, 109-245 U/L) and alpha-hydroxybutyrate dehydrogenase (223, 72-182 U/L) levels was observed. The triple repeat numbers of Huntington’s disease gene exon 1 and spinocerebellar ataxia types 1, 2, and 3 were all within in the normal range. The absence of chorein in erythrocytes was detected by Western blotting. Symptom Checklist-90-Revised test yielded normal results while the mini- mental state examination showed a mild decrease (28 points).

Figure 1: Cerebral blood flow perfusion SPECT-CT imaging. A) Cerebral blood flow perfusion SPECT imaging of the whole brain; B) intact skull continuity of the patient from his brain CT imaging; C) brain CT of basal ganglia area; D) 99Tcm-TRODAT-1 SPECT brain hybrid fusion imaging of basal ganglia area; E) integration of brain CT and SPECT image, indicating that the cerebral blood perfusion was significantly reduced in bilateral caudate nucleus and slightly decreased in the corpus striatum and thalamus, but experienced no significant changes in other brain areas.
Figure 2D), susceptibility weighted imaging (SWI, Figure 2F), and time-of-flight MR angiography (TOF-MRA, Figure 2H) showed any significant abnormalities except for atrophy of caudate nucleus and mildly dilated anterior horns of bilateral lateral ventricle. The volume of caudate nucleus was significantly decreased (by 39.43%) compared to those of age-and sex-controlled subjects (analyzed by MATLAB software package). The MR spectrum (MRS) manifested a decreased NAA/Cr ratio and increased Cho/Cr ratio in the bilateral caudate nucleus areas (Figure 2 I,J,O). The data indicated neuronal loss (reduction of NAA/Cr ratio), possible reactive glial activation (increased Cho/Cr ratio) and normal membrane turnover (normal mI/Cr ratio, data now shown) in these brain areas.

DISCUSSION

In this study, we showed that SPECT-CT and MRS tests enabled the early diagnosis of this NA case. An earlier study found increased myo-inositol (mI)/Cr and Cho/Cr ratios and normal NAA/Cr ratio in the putamen and globus pallidus of two siblings with NA. A recent MRS study revealed normal Cho/Cr ratio, decreased NAA/Cr ratio, and increased mI/Cr ratio at the level of the basal ganglia in one NA patient, while normal Cho/Cr and NAA/Cr ratios and decreased mI/Cr ratio in another NA patient. These results differ from ours showing decreased NAA/Cr ratio and increased Cho/Cr ratio in the putamen and caudate nucleus areas. Our data indicated neuronal loss (reduction of NAA/Cr ratio), possible reactive glial activation (increased Cho/Cr ratio) and normal membrane turnover (normal mI/Cr ratio, data now shown) in these brain areas. The different MR equipment, the course of the disease, small sample size,
image post-processing might have contributed to the variation in these results.

In summary, NA disorders are extraordinarily rare and very likely to be misdiagnosed or underdiagnosed. Our SPECT-CT data showed a significant reduction of blood perfusion in caudate nucleus and MR indicated reduced NAA/Cr ratio and increased Cho/Cr ratio in caudate nucleus. The combination of SPECT-CT and MR techniques, which integrates the advantages of functional imaging (SPECT-CT) and multiplanar capabilities plus excellent contrast of soft tissue (MR), might enable the early diagnosis of NA syndromes, although with variable MRS endophenotypes from different studies at this point.

CONSENT

Written informed consent was obtained from the patient and his parents for publication of this Case report and related images. A copy of the written consent is available for review by the Series Editor of this journal. All clinical investigations have been conducted according to the principles expressed in the Declaration of Helsinki.

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AUTHORS’ CONTRIBUTIONS

XL, NX, KG, QZ, XL, ZL, TW, ZHL, XQK, CL contributed to the conception and design. XL, NX, KG, QZ, CL took care of collecting the clinical information. XL, NX, XL, KG, CL, XQK analyzed and interpreted the MR and SPECT-CT data. XL, NX, KG, ZL, ZHL, TW, XQK, CL coordinated and helped to draft the manuscript. All authors have read, revised and approved the final version of the manuscript. XLo, NX, KG equally contributed to the work.

REFERENCES