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Canavan Disease- a rare Leukodystrophy

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Abstract

Canavan disease, also called Canavan–van Bogaert–Bertrand disease, is an autosomal recessive leukodystrophy that causes progressive damage to nerve cells in the brain and caused by a deficiency of the enzyme aminoacylase 2. A 22 years old male patient was presented in Department of Radiology and Imaging, Khwaja Yunus Ali Medical College and Hospital, Sirajganj with the complains of progressive weakness of all four limbs and gait disturbance since birth. On CT scan, it was revealed that diffuse hypointensity along white matter, subcortical arcuate fibers sparing thalamus and basal ganglia with thinning of cortex without any significant contrast enhancement. From the imaging findings and clinical presentations, the patient was diagnosed as a case of leukodystrophy and according to distribution of white matter ischemia, ultimately the patient was diagnosed as a case of Canavan disease. Although this is very rare disease, radiologist should be aware of this type of leukodystrophy so that patient is diagnosed properly and get adequate management.

Key words: *Canavan disease, Leukodystrophy, MRI*

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Introduction

Canavan disease, is an inherited genetic abnormality due to lack of an essential enzyme aminoacylase 2, causes destruction of myelin in the brain, thereby preventing the proper transmission of nerve signal.[1-3] Symptom appears in children between 3 to 6 month of age including developmental delay, significant motor slowness, enlargement of head (macrocephaly), loss of muscle tone (hypotonic), poor head control and severe feeding problem.[4] As the disease progresses seizures, shrinkage of the nerve of the eye (optic atrophy) and developed often blindness, as do heart burn (gastro-intestinal reflux) and deterioration of the ability to swallow. Canavan disease is inherited as an autosomal recessive condition with both parents silently carrying a single Canavan gene and each of their children

running about 25 % risk of receiving both genes and having the disease. Canavan disease is more prevalent among individuals of eastern European Jewish back-ground, then in others.[1,2,5] Canavan disease is caused by a defective ASPA gene which is responsible for the production of enzyme aspartoacylase. Decrease aspartoacylase activity prevents the normal break down of N-acetylaspartate, where in the accumulation of N-acetylaspartate or lack of its further metabolism interferes with growth of the myelin sheath of the nerve fibers of the brain. The myelin sheath is the fatty coverings that surround nerve cells and acts as insulator which allows for efficient transmission of nerve impulse.[5-7] On imaging, non-contrast CT scan shows diffuse low density throughout the cerebral white matter with normal sized ventricles. T1 wieghted scans in infantile Canavan Disease demonstrate homogeneous diffuse, symmetric low signal intensities throughout the white matter. T2 weighted images show near total high signal intensity in the supratentorial white matter. The subcortical arcuate fibres are predominantly involved. Relative sparing of the internal capsules is seen in few a cases. The cortex may appear thin (Figure 1).[6-8]

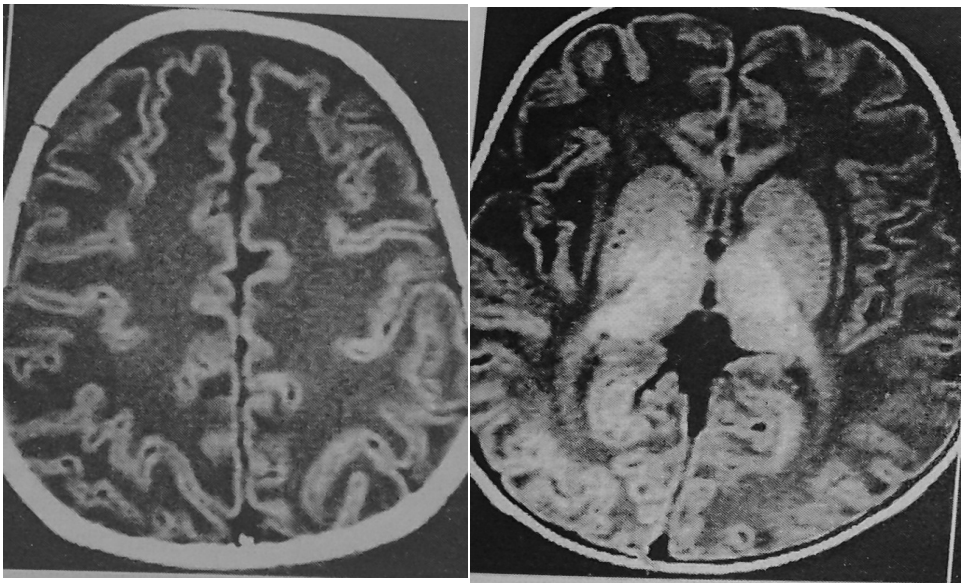

Figure 1: Non-contrast CT scan shows diffuse hypointensity along white matter, subcortical arcuate fibres sparing thalamus, basal ganglia with thinning of cortex

No definite treatment is present for Canavan disease. In addition, there is experimental trial of gene therapy, published in 2002, involving using a healthy gene to take over for the defective one that causes caravan disease. In human trials the results which were published in 2012. This method appeared to improve the life of the patient without long-term adverse effects during 5 years follow up. Death usually occurs before age 10 years but some children with milder forms of the disease survive up to their teen and 3rd decade.[3,5,7]

Case Report

A 22- years old male patient was presented with the complaints of progressive aesthenia of all

four limbs and gait disturbance since birth. On examination, muscle tone was decreased, GCS was 15/15, IQ was below average level (below 80). CT scan images demonstrated that diffuse hypointensity along white matter, subcortical arcuate fibre sparing thalamus, basal ganglia with thinning of cortex and normal sized ventricles without any significant contrast enhancement (Figure 2).

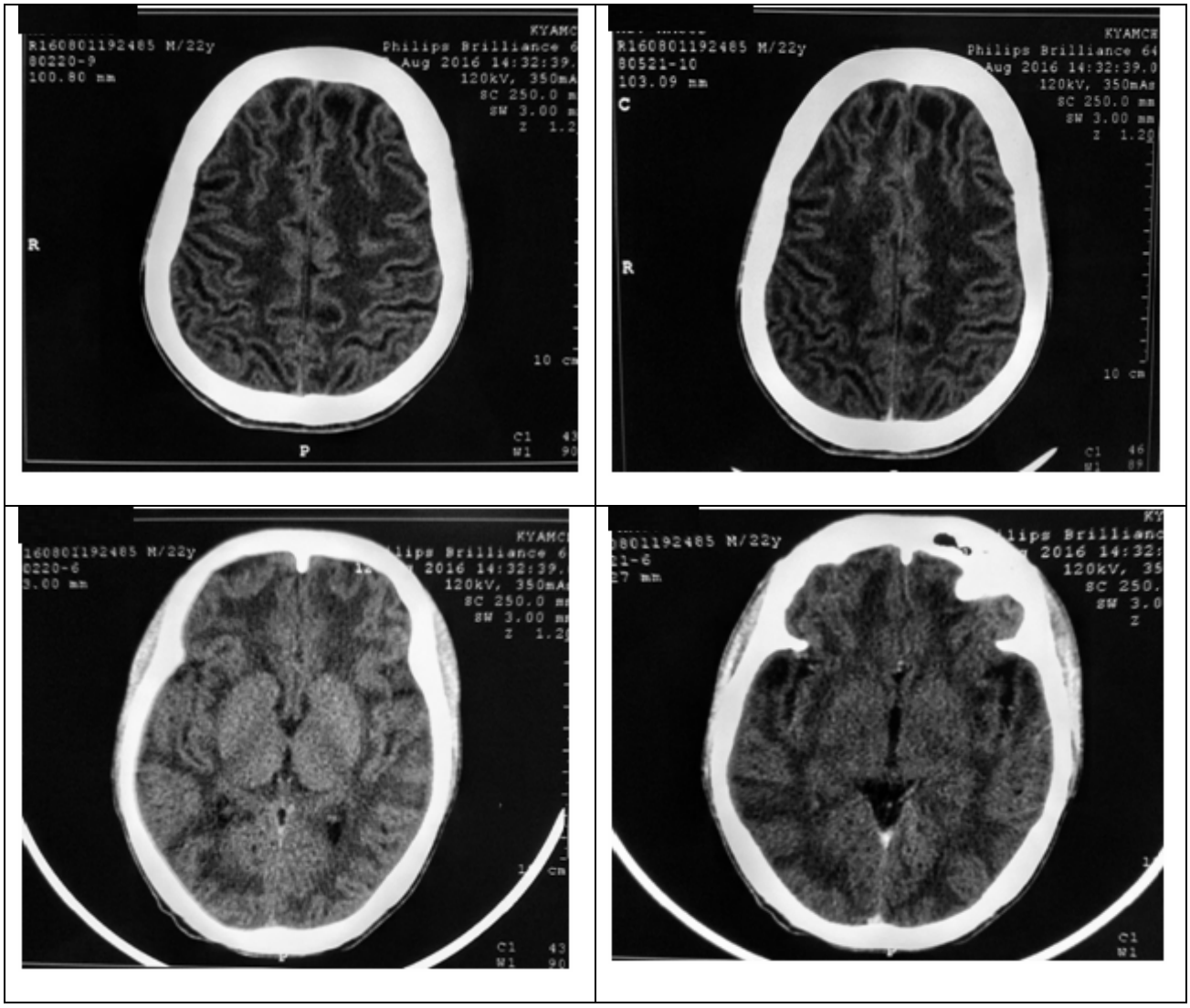

Figure 2: Non contrast and contrast CT of brain showing diffuse hypointensity along white matter, subcortical arcuate fibre sparing thalamus, basal ganglia with thinning of cortex and normal sized ventricles

MRI was advised but patient was unable to do it due to financial constrain. Considering the clinical presentations and imaging findings, the patient was diagnosed as a case of leukodystrophy and according to distribution of white matter ischemia; finally the patient was diagnosed as a case of Canavan disease.

Discussion

Canavan disease is a rare inherited disorder that damages the ability of neurons in the brain to send and receive messages. This disease is one of a group of genetic disorders called leukodystrophies.[1] Leukodystrophies disrupt the growth or maintenance of the myelin sheath, which is the covering that protects nerves and promotes the efficient transmission of nerve impulses. Neonatal/infantile Canavan disease is the most common and most severe form of the condition. Affected infants appear normal for the first few months of life, but by age 3 to 5 months, problems with development become noticeable. The mild/juvenile form of Canavan disease is less common. Affected individuals have mildly delayed development of speech and motor skills starting in childhood. These delays may be so mild and nonspecific that they are never recognized as being caused by Canavan disease.[3,4,6] Our had mild/juvenile form of Canavan disease as he crossed his infancy, had asthenia, hypotonia of all four limbs and gait disturbance since birth which was progressive. All the leukodystrophyies appear on imaging as diffuse hypodensity along white matter at CT scan and hyperintensity at T2 weighted MR imaging.[6] In present case of leukodystrophy, there was diffuse hypointensity along white matter, subcortical arcuate fiber sparing thalamus, basal ganglia with thinning of cortex. Previous researchers[5,6] observed that subcortical arcuate fibers are not affected in other leukodystrophy, where as in current case subcortical arcuate fibers were involved which favored Canavan Disease on imaging. Previous MR imaging[6] revealed thinning of cortex with normal sized ventricles in Canavan Disease. Similar findings were seen in our present case on imaging.

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