A Libyan case of Canavan disease

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Introduction

This disease is first described by Canavan in 1931, inherited as autosomal recessive trait with the gene mapped to chromosome No. 17p13 (short arm of ch 17 at the locus 13) which codes for the enzyme aspartoacylase that hydrolyse N-acetylaspartic acid to L-aspartic acid (1), in the series of Kaul 12 of 17 cases have point mutation while the remainder have compound heterozygous state.

The condition is fairly rare with the exception of Ashkenazi jews in whom the carrier state is about 1 in 40, in most cases symptoms appear as early as second month of life with hypotonia optic atrophy and lack of intellectual development with seizures later on, macrocephaly is noted by the age of 6 months and it was seen in all Arab cases reported by Gascon and colleagues, nystagmus and abnormal visual evoked potential is seen in most of the cases, death can occur from 5th birthday or delayed to third decade of life. Some have very slow progress and the clinical picture better than the radiological picture (child neurology by John H Menke) and as the two sisters that presented in this case report (1).

Case: Two Libyan girls (6 years and 4 years now) (the only children in the family) are product of normal vaginal delivery without any perinatal events of non-consanguineous marriage, with regular follow up during pregnancy, they were normal until the second month of age when they start to be floppy, poorly concentrating, hyperaccusis. In the last year, they develop generalized epilepsy which easily controlled by valproate.

Examinations: Both sisters have the same presentation and first examination shows: when they presented to me the older girl was about 3 years of age, she is fully conscious, oriented to her mother, no obvious cranial nerve problems, head circumference far above 95 centile, nystagmous, squint, clear hypotonia (frog like posture, slips on vertical suspention) hyperreflexia, and marked psychomotor developental delay, optic atrophy. The younger examination is almost the same.

Figure 1: Libyan girl with Canavan disease

Investigations: MRI: two MRI scans were done with about three years interval shows the disease progress radiologically. The first MRI shows hyperintensity of hemispheric white matter in T2W1, early involvement of subcortical U fibers which reflects spongy degeneration and demylination.

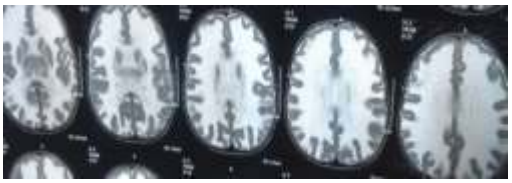

Fig. 2: MRI after few years showed marked degeneration and vaculation

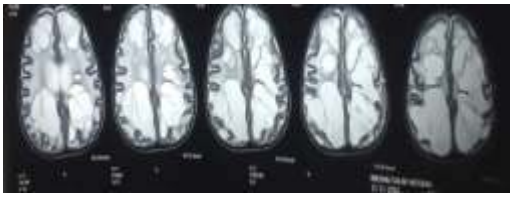

Fig. 3: Shows the severe damage in the brain

Laboratory findings showed marked increase of N-acetylaspartate in urine and plasma which gives the diagnosis of Canavan disease with the typical radiological picture.

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Discussion

N-acetylaspartate present in neurons, its function is not fully understood, but may be it serves as source of the acetyl group needed for the synthesis of myelin lipids. The cause of neurological deterioration may be because that accumulation of NAA leads to osmoregulatory disturbance that destroys the brain substance.

Differential diagnosis: Alexander disease: more slowly progress with predilection of frontal white matter in MRI. Megalencephaly with leukoencephaly and cyst MLC: subcorticasl cyst, normal basal ganglia, normal n-acetylaspate. Pelizaeus Merzbacher disease: proofund deficiency of myelin since birth, more rapidly progressive, normal n-acetylaspartate, can be diagnosed by detection of PLP gene.

Conclusion: Canavan disease is neurodegenerative white matter disorder that causes serious out come without any known treatment till now and the only way to decrease the family burden is not to have the disease from the start and this will occur only with family planning and diagnosis of the disease in the families help in this issue also by education that the disease occurs more in consanguineous marriages.

References

1. Menkes JH (2006) Child neurology 7th ed: Lippincott. UK