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Letter to the Editor

Are we missing fucosidosis?

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Fucosidosis is a rare lyosomal storage disease (LSD) with an autosomal recessive mode of inheritance. Clinical phenotype includes coarse facial features, hepatosplenomegaly, progressive neurological deterioration and angiokeratoma. Almost all LSD share these features except angiokeratoma which is a main differentiating feature found also in Fabery disease. The aim of this letter is to highlight the specific signs of fucosidosis and the difficulties in diagnosis of this LSD.

Our patient is a 2-year-old boy, the second in birth order of first cousins parents. He had a similar affected sister who died at the age of 4.5 years without a definitive diagnosis. The child was born full term after uncomplicated pregnancy and had normal development of motor and milestones till the age of 9 months when he started to lose previously acquired milestones and to develop abdominal distension. At the age of 11 months, he developed convulsions which responded well to sodium valproate. The parents also complaint from recurrent attacks of fever which was sometimes (but not all times) explained by chest infections. On examination, his weight was 10 kg (<−3 SD), length was 82 (−2 SD) cm and skull circumference was 50 cm (+1 SD). He had no coarseness of facial features. Abdominal examination revealed firm hepatomegaly (liver enlarged 4 cm below costal margin) with rounded border and smooth surface, non-correctable kyphosis and no angiokeratoma. Neurological examination revealed generalized hypotonia of all limbs and trunk, and increased deep tendon reflexes and preserved superficial reflexes. He had also limitation of movements of both ankle joints with shortness of tendoachilis. X-ray survey revealed dysostosis multiplex. His fundus and slit lamp examination revealed no abnormality. CT brain showed bilateral cerebral basal ganaglia and corona radiata calcifications, Fig. 1. MRI brain showed defective white matter myelination for age in the form of bilateral symmetrical abnormal high signal more of the deep cerebral white matter and internal capsules. Serum ammonia, lactate, extended metabolic screen, organic acids in urine, glucocerebrosidase, sphingomyelinase, arylsulfatase enzymes assays were also normal. Total glucosaminoglycans (GAGS) in urine and alpha-L iduronidase was also normal. Alpha-L-fucosidase enzyme assay in leucocytes showed marked deficiency (2 nmol/h/mg protein while control sample was 52 nmol/h/mg protein) confirming the diagnosis of fucosidosis.

Reaching the diagnosis in this patient was difficult because the patient had neither coarse facial features, nor angiokeratoma in addition to the abnormal CT and MRI brain findings. The absence of angiokeratoma in our patient can be explained by the fact that its onset is usually at the age of 4 years and our patient was only two years old [1]. Coarse facial features and organomegaly could be also absent in some cases [1,2]. Absence of dysostosis multiplex in fucosisdosis has also been reported [3].

Although the demyelination and basal ganglia affection found in MRI brain of our patient was previously reported [4–7], it is not specific for fucosidosis and can be found in many neurodegenerative disorders and the calcification of basal ganglia further confusing the clinical picture especially when the patient do not have coarse facial features or angiokeratoma like our patient. To our knowledge, basal ganglia calcification has not been reported before.

The diagnosis becomes more difficult with adult onset forms. Fleming et al. reported a 46 year old lady with neuroregression, short stature, dysostosis multiplex, generalized muscle wasting and angiokeratoma corporis diffusum. The patient was unhappy in warm temperature and suffered from anhydrosis. One of the peculiar findings in fucosidosis is the presence of anhydrosis which explains the recurrent attacks of unexplained fever in our patient.

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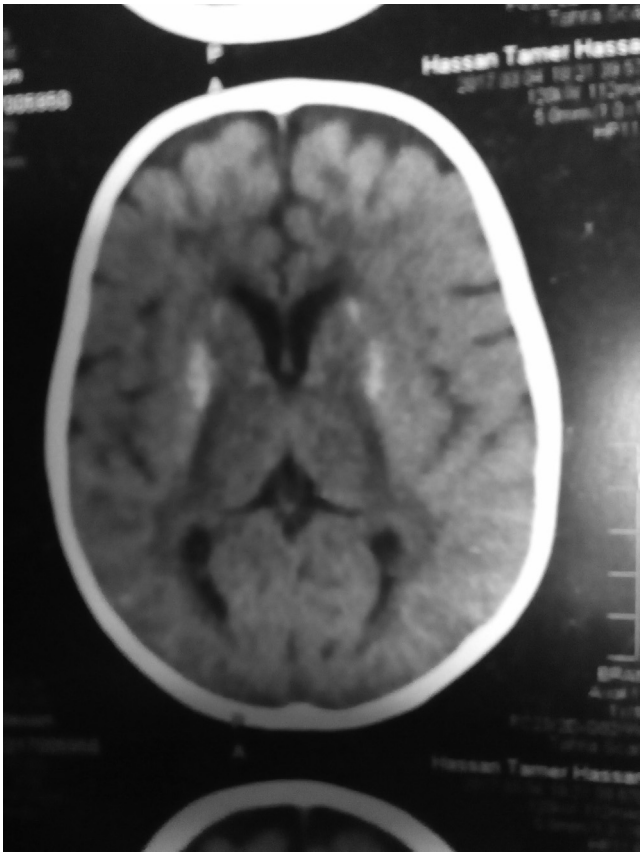

Fig. 1. CT brain showed bilateral basal ganaglia and corona radiata calcifications.

It is a well recognizable feature of this disorder and has been reported in different patient's age groups [8,9]. Anhydrosis together with clinical features of LSD in a patient with neuroregression is very suggestive of fucosidosis.

Willems et al. [10] reported interfamilial and intrafamilial clinical variability that do not correlate with the residual enzyme assay or genotype and suggested that environmental factors or modifying genes may contribute to the continuous clinical spectrum. This might explain the difficulties in diagnosis and highlights the importance of keeping in mind the diagnosis of fucosisdosis when examining a patient with neurodegeneration [10].

To conclude, fucosidosis has broad clinical spectrum and similarities to many LSD and neurodegenerative disorders. Angiokeratomas and anhydrosis is two characteristic features that should alert the physician to think of fucosidosis in patients with neurodegeneration. Basal ganglia calcification is a new finding in this disorder.

Declaration of Conflicting Interests

The author declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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