Type 2 Gaucher's disease in a Malian family

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Summary

Gaucher's disease is a recessive autosomal disorder caused by an inherited deficiency of betaglucocerebrosidase. We report here the case of an 8 month old child, fourth in a family of four children, who presents the neuropathic form of the disease. The dosages of betaglucosidase activity using C14 techniques have confirmed the diagnosis, and allowed the detection of the disease in the elder brother. Both parents were considered as responsible for the transmission of this disease to their progeny. The type 2 Gaucher's disease is rare in black population, and may be associated with phenotypes heterogeneity.

[Afr J Health Sci 2004 ; 11 : 67-69]

Introduction

Gaucher's disease is a recessive autosomal disorder caused by an inherited deficiency of betaglucocerebrosidase (a lysosomal enzyme). A deficiency of this enzyme induces an accumulation of the glucocerebroside in the liver, spleen, bone marrow and very often the entire reticuloendothelial system [1,2,3]. According to the presence and progression of neurologic symptoms, three clinical varieties of Gaucher's diseases have been described [2]. Type 1 represents the most common clinical form. It may be associated with a tremendous phenotypic heterogeneity, ranging from clinically asymptomatic to massive hepatomegaly, hypersplenism growth retardation in children and extensive involvement of bone and lungs [4]. Type 1 shows no neurological involvement. Type 2 is rare and more severe than type 1. It causes a neuropathy with nerve cell destruction within the central nervous system, causing an acute brainstem dysfunction or progressive neurologic deterioration. Patients usually die before the age of two years. Type 3, also called the juvenile form of the disease is characterized by a progressive development of uncompensated neurological functions that occur through adolescence or by adulthood. A comprehensive literature review enabled us to identify a few isolated cases of no-neuropathic forms from South Africa [5,6,7,8]. To our knowledge, the type 2 neuropathic form of Gaucher's disease has never been described in a black African family. We report here the first case of Type 2 Gaucher's disease from a Malian family.

Case Report

Observation 2305/98 B: Female, 8 months of age, hospitalized at the Neurology Unit of the Hospital Point G, Bamako, Mali, for psychomotor regression. She is the 4th of 4 siblings. There was no abnormal circumstance associated with birth or delivery that was reported by her parents. The child weighed 3 kg at birth. Clinical history revealed a normal psychomotor over the first 5 months after birth. At 6 months of age, the mother irritability, the fontanels were incompletely closed and a tonus disorder: Wile seated, the child could not

keep her head upright and observed nightly abdominal pains associated with alternating diarrhea and constipation. At hospital admission, clinical examination revealed a certain exhibited an opisthonos-extension of the neck when lying on her back. The upper limbs were bent and the lower limbs stretched. The osteo-tendon reflexes were abnormally sharp. In addition to these neurological symptoms, hepatomegaly and a pale conjunctiva were also observed. The fundus ocular exhibited a temporal pallor. A Trans fontanel ultrasound scan was normal; a whole body scan was not performed. An EEG revealed angular theta anomalies focused in the average and posterior temporal regions. A diagnosis of Gaucher's disease was made based on the above clinical observations. Biochemistry abnormalities were assessed from a blood sample collected in a tube containing EDTA. Biochemistry tests included assays of the leucocytes. The results from the patient and her parents are summarized in Table 1:

Table 1: Biochemistry tests in the patient and her parents (nm/mg of protein/ H)

	Betaglucosidase	Phosphatase Acid	Chitotriosidase
Patient	2.7	2000	44500
Patient's Brother	8	224	-
Father	12.6	-	-
Mother	12.0	-	-
Control	**32**	**152**	**47**

The concentrations of the glucocerebrosidase in the patient's parents were 12 nm/mg of protein/H for the mother and 12.6 for the father. The abnormal biochemistry results together with the neurological impairments and the death of the patient in her 10th month anniversary are consistent with a diagnosis of the Type 2 Gaucher's disease. No autopsy was performed.

Discussion

Patient medical history, physical examination, clinical symptoms and biochemistry profile enabled us to identify Gaucher's neuropathic disease, type 2. The occurrence of symptoms over the first 6 month of life, dramatic decrease of betaglucosidase (2.7) activity together with a significant increase of acid phosphatase (2000), are consistent with the diagnosis of type 2 Gaucher's disease. Usually, death occurs by the first anniversary of birth with the type 2 form of the disease. The Type 2 form is clearly rare, representing only 1% of Gaucher's disease [9]. Currently, the diagnosis of the disease requires an assay of betaglucosidase activity. Therefore, the elder brother of the patient who did not show any symptoms of the disease was tested to determine the activity level of leucocyte betaglucosidasidase and plasma acid phosphatase. The results of these tests also were consistent with a diagnosis Gaucher'sdisease and may be the expression of a different phenotype. Using C14- labeled glucocerebroside as substrate, the mother's leukocyte extract exhibited glucocerebrosidase activity of 12.0 nanomoles of glucocerebroside cleaved/mg protein/hour which is 70 % of the Narobi controls (18.0; 16.2; and 17.1 ; average: 17.1). The father's leukocyte extract exhibited glucocerebrosidase activity of 12.6 nanomoles of glucocerebroside cleaved /mg protein/hour which is 74% of the Narobi controls. Based on these results, we concluded that both parents are carriers of the mutated gene. A large heterogeneity in

the non- neuropathic form of Gaucher's disease has been documented, ranging from asymptomatic to a massive hepatosplenomegaly associated with involvement of bones and lungs [4]. This case report raises the possibility of phenotypic heterogeneity in the type 2 manifestation of the disease. The potential role of the environment, ethnicity and genetic background in the natural course of the disease [9] calls for more investigation in this geographic area to assess the prevalence and the importance of the phenotypes of Gaucher's disease in black African populations.

Conclusion

Although type 2 Gaucher's disease is rare in black populations, it may be associated with phenotypes heterogeneity.

Acknowledgments

We would like to thank and acknowledge Brady Roscoe (NINDS) for his invaluable input and Catherine Caillaud (Hopital Cochin, Paris) for her assistance in testing for the biochemical abnormalities.

References

1. Morales LE. Gaucher's disease : a review. *Annals Pharmacotherapy.* 1996; **30**(4) :381-388.
2. Tsai FJ; Lee CC; Wu McLinSP; Lin CY;, Tsai CH; Kodama H; and Wu JY. Mutation analysis of type II Gaucher's disease in five Taiwanese children: identification of two novel mutations. *Acta Paediatric Taiwan.* 2001; **42**(4) :231-235.
3. Schaison G ; Caubel I ; Belmatoug N ; Billette de Villemeur T ; and Saudubray JM. French results of enzyme replacement therapy in Gaucher's disease. *Bulletin de l'Academie Nationale de Medecine.*2002; **186**(5): 851-861.
4. Elstein D; Abrahamov A; Dweck A; Hadas-Halpern I and Zimran A. Gaucher's disease: pediatric concerns. *Paediatric Drugs.* 2002; **4**(7): 417-426.
5. Morar B and Lane AB. The molecular characterization of Gaucher's disease in South Africa. *Clinical Genetics.*1996; **50**(2): 78-84.
6. Patel R and MacDougall LG. Gaucher's disease in a black child in South Africa : A case report. *South African Medical Journal.* 1984; **66** (9): 343-344.
7. Jacobs P; Tribe R; Petersen EM and Bergerton P. Gaucher's disease in the black population of South Africa. A case report. *South African Medical Journal.* 1983; **64**(13): 490-492.
8. Goldblatt J and Beighton P. Gaucher's disease in South Africa. *Journal Medical Genetics.* 1979; **16** (4): 302-305.
9. Charrow J; Andersson HC; Kaplan P; Kolodny EH; Mistry P; Pastores G; Rosenbloom BE; Scott CR; Wappner RS; Weinreb NJ and Zimran A. The Gaucher registry: demographics and disease characteristics of 1698 patients with Gaucher's disease. *Archives Internal Medicine.* 2000; **160** (18): 2835-43.