Prenatal Diagnosis of Gaucher Disease

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Introduction

Gaucher disease (GD) is a rare disease but is the commonest enzyme deficiency disorder among the group of inherited lysosomal storage diseases [1]. It is caused by a deficiency in glucocerebrosidase (a lysosomal enzyme also referred to as acid beta-glucosidase) or, in rare cases, by a deficiency in the activator protein saposin C. Following genetic counselling and informed consent, direct enzymatic assay of acid beta-glucosidase on chorionic villi samples (CVS) can be offered to families in which GD has been diagnosed. We report prenatal diagnosis of GD by CVS in a couple with one child suffering from GD Type 1.

Case Report

A two years old male child born of consanguineous marriage of a couple residing in Rajasthan was referred to the paediatric department of our hospital for progressive abdominal distension, hepatomegaly and failure to thrive of one year duration. Clinical examination and laboratory investigations were suggestive of a storage disorder. The child was tested for blood glucocerebrosidase activity which was found to be absent, so he was diagnosed as a case of GD Type 1 since there was no neurological deficit. At this time the mother was pregnant at 12 weeks of gestation and was referred to foetal medicine unit of our department for genetic counselling. After detailed counselling of the couple, they opted for prenatal diagnosis. CVS was done at 86 days of gestation for prenatal diagnosis of GD. Enzyme assay of chorionic villous for acid beta glucosidase was 1.55 nmol/hr/mg (Normal range 108-145nmol/hr/mg). In the CVS, one more enzyme, i.e. arylsulphatase A was estimated and was found to be normal. This indicated that the fetus was affected and parents opted for abortion of fetus which was done using prostaglandin. Following termination, villous material was sent for culture which also revealed enzyme deficiency (acid beta-glycosidase 1.35 nmol/hr/mg) thus reconfirming the diagnosis of GD.

Discussion

Gaucher disease is an autosomal recessive disorder, the gene for which is located on the 1st chromosome. In 1882, Phillipe Gaucher, a French physician, described this clinical disorder that bears his name. The prevalence of symptomatic disease is 1: 100,000. The underlying cause is a deficiency of glucocerebrosidase, a lysosomal hydrolase involved in the stepwise degradation of complex glycosphingolipids [2]. GD is classified based on clinical characteristics into three types: Type 1 is non neuropathic and the most prevalent with wide spectrum of presentation, Type 2 acute neuropathic and Type 3 chronic neuropathic [3]. Diagnosis of GD is based on assay of glucocerebrosidase activity in peripheral blood leucocytes or cultured fibroblast. Normally GD patients have enzyme activity that is significantly lower than normal (less than 30%) [4]. Clinical expression is remarkably variable in the Type 1 (non neuropathic) form. Disease progression is also unpredictable and can occur at any age. More than 300 mutant alleles have been identified. Presence of at least one N370s allele is associated with Type 1 disease and usually excludes neuropathic involvement. An important role of genotyping relates to screening and genetic counselling of the patient's family. The identification of carriers can be done by enzyme assay and molecular studies [5]. Testing should be offered to all family members, keeping in mind the great heterogeneity of the disease process.

Prenatal diagnosis for GD is now available at many centres. Parents should be counselled about the 25% risk of recurrence and the availability of prenatal diagnosis by enzymatic assay in CVS at 10-12 weeks of gestation or amniotic cell culture at 15-18 weeks. Carrier and prenatal testing for people with family history of GD should be offered in conjunction with genetic

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counselling so that people can be aware of available options and can make informed decisions [6]. Enzyme replacement therapy is now available for patients of GD in particular, Type 1 patients, who have anaemia, low platelet count, spleen enlargement, liver enlargement and bone disease. The current existing cost of enzyme replacement therapy (injection imiglucerase) is up to \$550,000 annually for a single patient and the treatment is to be continued for life. The couple should be informed about this during counselling for prenatal diagnosis. Aim of this case report is to apprise health care providers about the availability of prenatal diagnosis for GD in our country.

Conflicts of Interest

None identified

References

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Journal Scan

Corine M Koopmans, Denise Bijlenga, Henk Groen and others, for the HTPITAT study group. Induction of labour versus expectant monitoring for gestational hypertension or mild preeclampsia after 36 weeks' gestation: a multicentre, open label randomized controlled trial. www.thelancet.com Published online 2009; DOI: 10.1016/S0140-6736 (09) 60736-4.

Genuine evidence to guide direct management of pregnant women with mild hypertensive disease at term is scarce. The authors investigated whether induction of labour in women with a singleton pregnancy complicated by gestational hypertension or mild pre-eclampsia reduces severe maternal morbidity. They undertook a multicenter, parallel, open label randomized controlled trial in six academic and 32 non academic hospitals in the Netherlands between October, 2005 and March, 2008. Patients who had a singleton pregnancy at 36-41 weeks gestation, and had gestational hypertension or mild pre-eclampsia were enrolled. Participants were randomly allocated in a equal ratio by block randomization with a web-based application system to receive either induction of labour or expectant monitoring. The primary outcome was a composite measure of poor maternal outcome-maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thromboembolic disease, and placental abruption), progression to severe hypertension or proteinuria, and major post-partum haemorrhage (>1000 mL blood loss). Analysis was by intention to treat and treatment effect is presented as relative risk. A total of 756 patients were allocated to receive induction of labour (n=377

patients) or expectant monitoring (n=379). Out of these, 397 patients refused randomisation but authorized use of their medical records. Of women who were randomized, 117 (31%) allocated to induction of labour developed poor maternal outcome compared with 166 (44%) allocated to expectant monitoring (relative risk 0.71, 95% CI 0.59-0.86. $p<0.0001$). No cases of maternal or neonatal death or eclampsia were recorded. To conclude induction of labour is associated with improved maternal outcome and should be advised for women with mild hypertensive disease beyond 37 weeks gestation.

In our service hospitals, 5-8% of pregnancies are complicated by hypertensive disorders. Such disorders in pregnancy make a substantial contribution to maternal and neonatal morbidity and mortality. Most hypertensive disorders present after 36 weeks' gestation. The results of this trial is important for our conditions. The finding that induction of labour was associated with a reduced risk of severe hypertension of HELLP syndrome and subsequent reduced need for caesarean section, emphasizes the importance of frequent blood pressure monitoring during the concluding weeks of pregnancy. Induction of labour should be advised for women with gestational hypertension and a diastolic blood pressure of 95 mm Hg or higher or mild pre-eclampsia at a gestational age beyond 37 weeks for better maternal and fetal outcome.

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