The Egyptian Journal of Medical Human Genetics (2015) 16, 159–163

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The Egyptian Journal of Medical Human Genetics

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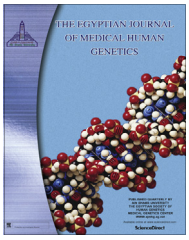

ORIGINAL ARTICLE

Prenatal genetic testing, counseling and follow-up of 33 Egyptian pregnant females with history of mucopolysaccharidoses

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Received 14 January 2015; accepted 29 January 2015
Available online 21 February 2015

KEYWORDS

Mucopolysaccharidosis;
Alpha-fetoprotein;
Amniotic fluid;
Glycosaminoglycans

Abstract *Background:* Mucopolysaccharidoses (MPS) are autosomal recessive disorders characterized by deficiency of lysosomal enzymes which break down the glycosaminoglycans (GAGs) which results in widespread intra and extra-cellular accumulations of GAGs. Early initiation of treatment, before the onset of irreversible tissue damage, clearly provides a favorable disease outcome. Early detection might be afforded by analysis of amniotic fluid.

Aim: To report our experience of prenatal diagnosis of MPS over 14-year period for cases referred from medical centers throughout Egypt. Also to report the benefit of prenatal genetic testing in cases accompanied with genetic disorders.

Materials and methods: The present study included 33 pregnant women at risk of having a fetus with MPS. Of these cases, 3 women had more than one pregnancy evaluated. All cases had a detailed genetic ultrasound examination and a maternal serum alpha-fetoprotein (MSAFP) evaluation during the second trimester of pregnancy. Thirty-eight amniocentesis procedures were performed during the study for 2 dimensional electrophoresis (2-DEP) of GAGs.

Results: Positive consanguinity was present in near 70% (23/33) of the couples. Detailed genetic ultrasound examination revealed a case with anencephaly and another one with a twin pregnancy.

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Peer review under responsibility of Ain Shams University.

http://dx.doi.org/10.1016/j.ejmhg.2015.01.004

One case had a MSAFP of 3.6 multiple of the normal median (open neural tube defect). Another 2 cases had a risk of having Down syndrome. Results of the 2-DEP of GAGs in amniotic fluid revealed 36.8% (14/33) affected fetuses. During the final counseling setting of the 14 cases with abnormal results, 43% (6/14) elected to continue their pregnancy while 57% (8/14) elected termination.

Conclusion: Early prenatal screening and diagnosis, through a systematic multidisciplinary approach, to all cases of mucopolysaccharidoses are recommended, to improve the quality of life and to avoid the presence of other associated fetal developmental malformations.

1. Introduction

Mucopolysaccharidoses (MPS) are autosomal recessive disorders characterized by deficiency of lysosomal enzymes which break down the glycosaminoglycans (GAGs). Their deficiency results in widespread intra and extra-cellular accumulations of GAGs [1]. They have been subdivided according to enzyme defect and systemic manifestations [2].

Together with the lipidoses, MPS are the most common lysosomal storage diseases. The overall incidence of each group is in the region of 1:10.000 births [3].

Early initiation of treatment, before the onset of irreversible tissue damage, clearly provides a favorable disease outcome. However, early diagnosis is difficult due to the rarity of these disorders in combination with the wide variety of clinical symptoms. Thus, much interest exists in prenatal detection by amniocentesis. Early detection might be afforded by analysis of amniotic fluid because it contains fetal urine and cells which commensurate with fetal age [4].

Prenatal genetic testing occurs in clinical settings, usually as part of obstetric care. The prenatal screening is the first step toward prenatal diagnosis of congenital malformations [5]. Prenatal genetic testing has initiated a great debate about reporting findings identified by a screening test to a population booked for a specific diagnostic test [6]. However, the primary purpose of prenatal testing is to gain information about the health of a fetus that may be at increased risk for a chromosomal or other genetic condition [7]. This is in addition to relieving parents' anxiety over inheriting a genetic disease or giving birth to a child with congenital abnormalities and this is the major outcome [6,7].

The purpose of this study is to report our experience of prenatal diagnosis of mucopolysaccharidosis over 14-year period (2000–2014) for cases referred from medical centers throughout Egypt. Also we will emphasize on the importance and role of prenatal genetic testing in all pregnancies, in screening for accompanied genetic disorders, even in cases where prenatal diagnosis is tailored to a specific disorder.

2. Patients and methods

2.1. Patients

This retrospective study was conducted at the Prenatal Diagnosis and Fetal Medicine Department and Biochemical Genetics Department, National Research Centre, Egypt, over a period of 14 years (2000–2014).

The study included 36 pregnancies (14–22 weeks gestation) in 33 families where a diagnosis with one of the MPS types has been made in one or more of their previous children. The exclusion criteria included previous cases with MPS IV.

The work was carried in accordance with the code of ethics of the world association (declaration of Helsinki) for experiments involving humans. A written informed consent was obtained from all pregnant women included in this study after full explanation of the study. The ethical approval was obtained from the medical ethics committee at the National Research Centre.

2.2. Methods

All cases in this study were subjected to:

- History taking, pedigree construction and clinical examination.
- Two counseling settings: The first entailed detailed explanation of the condition to be studied and the investigations to be carried. The second one included detailed explanation of the results and options to be carried by the parents.
- Detailed genetic ultrasound examination at time of presentation during the second trimester. This was done for detection of multiple pregnancies, placental location, fetal growth, soft tissue markers and the presence of associated fetal abnormalities.
- Measurement of maternal serum alpha-fetoprotein (MSAFP): 5 cc venous blood was collected during the second trimester of pregnancy ($15\,\text{weeks}^{+0}$–$18\,\text{weeks}^{+6}$). It was measured in duplicate using commercially available enzyme immunometric assay kit (EIA) Can Ag Diagnostics, Sweden. The values were transformed to multiple of the normal median (MoM) after adjusting the gestational age. A MSAFP above 2.5 MoM (cutoff limit) was considered elevated and carries a high risk for open neural tube defects, and the case was offered a second detailed ultrasound examination, if not detected before. MSAFP MoM was evaluated according to gestational age and older maternal age at the expected time of delivery for risk of Down syndrome. A risk of 1:270 or more was considered elevated, and the case was offered the opportunity for amniotic fluid study for fetal chromosomes.
- Extraction of GAGs from cell-free amniotic fluid: The amniotic fluid samples were centrifuged and the supernatants were taken and used for the extraction of GAGs by formation of complexes with alcian blue 8GX. In this procedure 3 ml of centrifuged amniotic fluid was mixed with