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Case Report Open Access

Normal Child by a Gestational Carrier of a Phenylketonuria (PKU) Mother-An Alternative to Diet

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Abstract

PKU mothers have a high incidence of spontaneous abortion. The consequences of untreated pregnancies are severely detrimental to their offspring. It manifested by intrauterine growth retardation with microcephaly, congenital malformations and abnormal intellectual development. Infants' pathology is independent of fetal genotype, but is directly correlated with excessive phenylalaninaemia of the mother throughout pregnancy. PKU mothers can produce healthy infant if they maintain a very restricted and controlled diet prior conception and during pregnancy. However to maintain a well-controlled diet prior to conception and during pregnancy is not possible in most cases, and significant mental and/or physical disability can result in children born due to either the delay or the not well controlled dietary treatment. We, previously, described the first child born using, non-PKU, gestational carrier with a PKU mother's egg and the husband's sperm. In this report, we present the normal developmental outcome of this infant at 4years 7 month of age. We suggest that doctors who take care of PKU females could suggest gestational carriers as an alternative therapy for MPKU.

Introduction

Maternal phenylketonuria (MPKU) is a well-established teratogenic syndrome of children born to mothers with phenylketonuria (PKU). The ill effects of MPKU include mental retardation, intrauterine growth retardation with mircocephaly spontaneous abortion, and congenital heart disease [1-4]. As many of the female PKU patients, grow into adulthood with good metabolic control, normal intelligence and good quality of life. The importance of having unaffected offspring becomes an important issue. The MPKU collaborative study has clearly demonstrated the fact that healthy birth outcomes occurred when maternal metabolic control was attained before or very early in pregnancy and maintained through pregnancy [5,6]. However this is not a simple task for many MPKU patients'. More importantly, many of the PKU patients of child bearing and rearing age do not keep regular contacts with the PKU centers. In a recent survey of long term follow up data collection of new born screen programs, it reported that older patients with disorders identified by newborn screening have very few follow ups [7]. Lee et al. [8] also suggested that the lack of appropriate resources to care for pregnant women with PKU may complicate the outcome of the pregnancies. Therefore, it would be very difficult to attain good metabolic control before pregnancy starts. Clarke et al. [9] suggested the need to explore novel and non dietary approaches to the treatment of MPKU. In 1993, Fisch et al. [10] recommended in vitro fertilization using gestational mother as an alternative therapy for MPKU. Subsequently, a normal male infant was born using gestational carrier for a PKU mother [11]. In this report, we present the developmental outcome of this infant at 4 years 7 month of age.

Method

The child was brought to the Pediatric Psychology Clinic for physical measurements, individual testing and parental interview. The following instruments were used.

Achenbach child behavior checklist (CBCL)

The CBCL asks the caregiver to rate the frequency and intensity of a variety of behaviors. Scores are summarized as T-Scores with 40-60 representing the average range. Scores above 70 are considered clinically significant [12].

Stanford-Binet intelligence scales–fifth edition

The Stanford-Binet Intelligence Scales is a measure of general intellectual functioning. It provides estimates of the individual's general verbal and non-verbal abilities, as well as, abstract reasoning, knowledge, quantitative reasoning, visual-perceptual and working memory abilities. Scores are presented as standard scores with 85 to 115 representing the average range [13].

Maternal history

The mother of this child was born in1975, she was considered as a "classical" PKU patient because her Phenylalanine (Phe) level was 2448 µ/l at 28 days of age when the diet was initiated. Diet was discontinued prior to 7 years of age. Her Phe level at the time of procedure was 1278 µ/l. The mother's last IQ score was 97 and she completed high school. Her gynecological history reveals one elective termination of pregnancy of 6 weeks' gestation, and right salpingectomy for ruptured right tubal pregnancy. She did not follow any diet. She has a close friend (22 years old who had a normal child) who agreed to become a gestational carrier.

Child's developmental status

Age: Four years and seven month.

Physical measurements

Height: 114 cm at the 95th percentile.

Weight: 20.5 kg at the 89th percentile.

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IQs and Indexes	Standard Scores
Verbal IQ	102
Non Verbal IQ	100
Full Scale IQ	101
Fluid Reasoning	88
Knowledge	97
Quantitative Reasoning	111
Visual-Spatial Reasoning	111
Working Memory	80

Table 1: The child's results are as follows.

Head circumference: 53.5 cm, at the 96th percentile.

Normal physical findings

Behavior assessment: The mother completed the Achenbach Child Behavior Checklist (CBCL) [12]. The child's mother did not report any behavior problems.

Intellectual assessment: The Stanford-Binet Intelligence Scales – Fifth Edition is a measure of general intellectual functioning. Scores are presented as standard scores with 85 to 115 representing the average range [13] (Table 1). The child's IQs are within the average range, using the 95% confidence interval his true Full Scale IQ is likely to fall within the range of 97 to 105. He does have relative weakness in the areas of working memory and fluid reasoning, falling at the borderline to low average range.

Discussion

It is known that children born to mothers who are untreated for PKU may suffer physical and/or intellectual deficiency. However children born to fathers with untreated PKU are without defects [14]. It is also known that concentration of maternal Phe level affects the fetus from conception to birth [15]. Direct correlation has been reported between the abnormality and Phe concentration [16,17]. In order to not affect the child, mothers with PKU have to be on a well-controlled diet throughout the entire pregnancy with the Phe level kept within normal range [5,6]. Additionally, Tyrosine (Tyr) deficiency also noted to lead to deficient brain protein synthesis [18]. Therefore, Tyrosine also needs to be controlled. Consequently, it is a difficult undertaking to maintain good dietary management for PKU mothers throughout their pregnancies. It requires determination on the part of the mothers with a supporting team of specialists in order to have successful dietary management. It is also known that as PKU patients advance in age, their dietary management becomes increasingly difficult [19]. Once the diet is terminated it is even more difficult to be reinstated. Despite the recommendations that "the diet is for life", only one-third of clinics follow patients beyond the age 18 years. Therefore, it is unclear how adult PKU patients' medical care was managed [14]. In MPKU, motivation and compliance were great challenges despite strong effort by the clinic staff [14,20]. There is strong correlation between PKU patients' IQ with the socio-economic status of their families, the quality of dietary control since birth, and the serum phenylalanine concentration [21]. It is reasonable to assume that those whose dietary control were poor in childhood and lost to long term follow up most likely will not seek or maintain appropriate diet during their pregnancy [14]. Currently, the outcome studies of offspring born to PKU mothers are only based on cooperative patients. Those PKU patients who have been lost to follow up or were unwilling to be followed are more likely to produce a much higher incidence of abnormalities in their offspring [21]. A study of the MPKU children shows that 44% have congenital abnormalities or developmental delay [22]. Considering all the factors that influence the concentration on Phe and tyrosine, i.e., daily amount of amino acid, protein and calories, disease, body temperature, activity, it is no wonder that children born to mothers treated for PKU are more likely reported to have abnormalities [23]. We do not have any data regarding PKU women who gave birth to children without being treated for PKU during pregnancy, or do we have the results of the outcome of the birth. But, we do know that the number of the PKU patients 'clinic visits decrease by age, and only one-third of clinics are providing care for patients beyond 18 years of age [14]. Therefore, there is a need for new approaches to try to reduce the birth of abnormal children of PKU mothers. We believe the use of gestational carrier is an alternative and should be suggested. Serious efforts have to be made to inform parents, the PKU patients as well as their future husbands and their families of the damaging consequences of maternal PKU. We also believe this information can also be given to patients at a younger age. Obviously, to find a volunteer woman who is willing to carry out someone else pregnancy is not an easy task either. But, the female member of the father's family can be possible candidates. Gestational carrier also require financial commitment, it is an expensive treatment of the PKU mothers. The insurance companies currently not only pay for mothers with PKU but also pay for the future medical expenses of their handicapped children. In this paper, it is clearly shown that the use of gestational carriers can have normal developing offspring, both physically and intellectually. However, there has no mention of this approach as a viable alternative in the medical literature. It is important that all PKU patients need to be made aware of the use of gestational carrier as a viable option for a heath offspring. We want to thank the young woman who gives life for friendship.

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