Phenylketonuria in a six year old Malay boy – A case report

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Summary
A six year old Malay boy with phenylketonuria is presented. The history, clinical examination, biochemical findings and treatment are described followed by a discussion on phenylketonuria.

Key words: Phenylketonuria, Malay boy.

Introduction
Phenylketonuria (PKU) is a genetic disorder caused by an inborn error in aromatic amino-acid metabolism resulting in mental retardation. Excess of phenylpyruvic acid in the urine was first described by Folling\(^1\) in 1934 and subsequently was named phenylketonuria by Penrose and Quastel. Jervis\(^2\) in 1953 identified the metabolic error and Bickel et al\(^3\) in 1954 reported the success of low phenylalanine diet therapy.

Very few cases of PKU have been described in this region: two cases have been reported in Chinese in Singapore\(^4\) and seven cases in Thailand.\(^5\) Although the incidence varies from 15–20 per 100,000 live births in Belgium and West Germany, to 5–9 per 100,000 live births in USA and Japan, we do not know the incidence of PKU in different ethnic groups in this region since systematic screening has never been carried out. We report here a case of PKU in a six year old Malay boy.

Case report
H.A.R a six year old Malay boy was referred to Hospital Universiti Sains Malaysia (HUSM) in January 1988 with the problem of aggressive behaviour and developmental delay. He was born in Mecca, Saudi Arabia after an uneventful pregnancy. His mother noticed at the age of three months that her child was rather quiet and could not hold his head up. He rolled over at eight months, sat without support at twenty months, walked at two years and talked with meaning at three years of age. At about one year old the mother noticed that his normal black hair gradually changed to light brown. There was no history of light hair on both parental sides. The child also had no history of fits or skin rashes. The parents were first cousins and one of the maternal grandfathers was mentally retarded. All their relatives were ethnic Malays.

Clinical examination revealed a stunted child with height and weight below the 3rd centile and with light brown hair. He was very playful, hyperactive and shouted whenever he wanted some-
thing. He was very destructive and aggressive towards other children. He could not follow simple instructions and was unable to read, write alphabetical letters or even perform simple arithmetics. The gross motor development was normal. Using the Seguin Form Board Test his mental age was assessed to be below 3.5 years old. Apart from mental retardation the neurological examination was normal. There was no evidence of eczema and rest of physical examination was normal.

Investigations revealed normal blood counts, blood glucose and electrolytes. The urine ferric chloride test was positive (blue-green) and dinitro-phenyl hydrazine test (ANPH) was also positive. The cyanide nitroprusside test was negative. Urine amino-acid thin layer chromatography (T.L.C) revealed a band of increased staining intensity which corresponded to the chromatogram of phenylalanine (Band 2 = phenylalanine). Plasma amino-acid chromatography (T.L.C) revealed the phenylalanine band (Band 2) was increased. These two tests were repeated in March 1988 with similar conclusions. The other siblings and the parents were screened but did not reveal any abnormality. Electroencephalogram and computerised tomography of the brain were normal.

In the management of this child we decided to embark on a low phenylalanine diet despite the late presentation for it was believed this diet could improve behaviour although not alleviate the mental retardation. We then followed up the child on this diet with the help of the dietician and community health workers for almost six months. However, the child could not co-operate because of the unpalatability and the parents though helpful could not afford the cost of the diet. We finally abandoned the special diet and concentrated on social rehabilitation and genetic counselling, with the help of the psychologist and community health workers.

**Discussion**

The history, physical examination and the repeated biochemical abnormalities strongly suggested PKU in this child. Testing the urine for phenylpyruvic and phenyllactic acids with ferric chloride together with a raised plasma phenylalanine level (T.L.C) usually confirm the diagnosis in symptomatic PKU.

PKU and hyperphenylalaninemia designate a group of inborn errors of metabolism of phenylalanine that results in elevated levels of phenylalanine in the serum and tissues (Fig. 1). The primary enzymatic defect may be localized to phenylalanine hydroxylase, dihydropteridine reductase or to one of the sequential enzymatic steps in the synthesis of the co-factor biopterin (Fig. 2). Several types exist (type I to VIII), all of which are autosomal recessive except type VI which is X-linked. Our child most likely has type I (classical) PKU which is due to deficiency of hepatic hydroxylase. The most important and consistent feature is mental retardation which is evident in our child in early infancy and later childhood. In untreated patients ninety-eight percent have an IQ less than 50. Other manifestations not present in our child included psychotic behaviour, dermatographia, “mousy” body odour, eczema and seizures.

In PKU the positive ferric chloride test (blue green) is due to the excess of phenylpyruvic and phenyllactic acids in urine resulting from deficiency of the enzyme phenylalanine hydroxylase. One has to be careful in interpreting the test because there are many false positive and false negative results. The Guthrie test (not available here) has revealed several variants of phenylalaninemia including the three benign variants which do not produce mental retardation. In classical symptomatic PKU there are two varieties: severe (plasma phenylalanine 50–100 mg/dl) and the less severe (plasma phenylalanine 30–50 mg/dl). Liver biopsy studies have confirmed the presence of these two varieties.
Fig 1: Plan showing various inborn errors of metabolism due to deficiencies of different enzymes in the breakdown of phenylalanine.
Low phenylalanine diet is the only practical measure at present but is fraught with numerous problems like unpalatability, diarrhoea and high cost. However, recently in 1976 Yamashita et al. have reported a method of preparing low phenylalanine peptide (LPP) which can be used not only as a more palatable therapeutic milk but also as an ingredient to make more palatable foods (soup, cakes, ice cream). A 'one-shot' cure of the disease remains elusive and may become available in the more distant future by somatic cell gene therapy. Prevention by prenatal diagnosis is not widely accepted in this region because of legal, religious and moral reasons. PKU has been thought to be very rare in this region and has not been reported in ethnic Malays. A prospective pilot survey is thus clearly needed to determine the incidence of this disease and the gene frequency before assessing the need, if any, for large scale routine screening.

References


