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CLASSICAL PHENYLKETONURIA ASSOCIATED WITH GOLDENHAR'S SYNDROME*

A Case Report

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SUMMARY: Tokatlı A, Coşkun T, Kocabaş CN, Özalp İ, Balcı S. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Classical phenylketonuria associated with Goldenhar's syndrome. A case report. Turk J Pediatr 1994; 36: 153-156.

Classical phenylketonuria (PKU) and Goldenhar's syndrome were diagnosed in a six-month-old male infant who was referred to Hacettepe Children's Hospital for evaluation of developmental delay. There had been epibulbar dermoids in his left eye, strabismus, bilateral multiple preauricular appendices, malar hypoplasia, micrognathia, hemifacial microsoma and high palatal vault. In addition to congenital anomalies and developmental delay, blond hair, fair skin and unusual urinary odor were noted. Ferric chloride test on his urine sample was positive, and the plasma phenylalanine level was high (34 mg/dl). Based on these clinical and biochemical findings, the diagnoses of phenylketonuria and Goldenhar's syndrome were made. To our knowledge, this is the first case with PKU and Goldenhar's syndrome. *Key words: classical phenylketonuria, Goldenhar's syndrome.*

Classical phenylketonuria (PKU), resulting from a deficiency of the hepatic enzyme phenylalanine hydroxylase (PAH), has been reported in association with some genetic and non-genetic diseases[1-9].

Goldenhar's syndrome (oculoauriculo-vertebral dysplasia) is characterized by epibulbar dermoids, preauricular appendages and pretragal fistulas. Several congenital defects have been reported with Goldenhar's syndrome[10-15].

This is the first report of PKU associated with Goldenhar's syndrome.

Case Report

The patient was the second child of healthy, non-consanguineous parents and born after an uneventful pregnancy and delivery with a birthweight of 2500 g. His sister was healthy. Certain anomalies were noted at the time of birth. There were small, round, creamy-white epibulbar dermoids in the medial limbus of the left

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eye, strabismus, bilateral multiple preauricular appendices, malar hypoplasia, micrognathia, hemifacial microsoma and high palatal vault (Figs. 1, 2). At six months of age, he was referred to Hacettepe Children's Hospital for evaluation of developmental delay. His weight was 7150 g. (75^{th} percentile), length 69 cm (75^{th} percentile) and head circumference 43 cm (25^{th} percentile). On physical examination, in addition to congenital anomalies and developmental delay, blond hair, fair skin and unusual urinary odor were noted. Ferric chloride test on his urine sample yielded a strongly positive reaction. The plasma phenylalanine level was

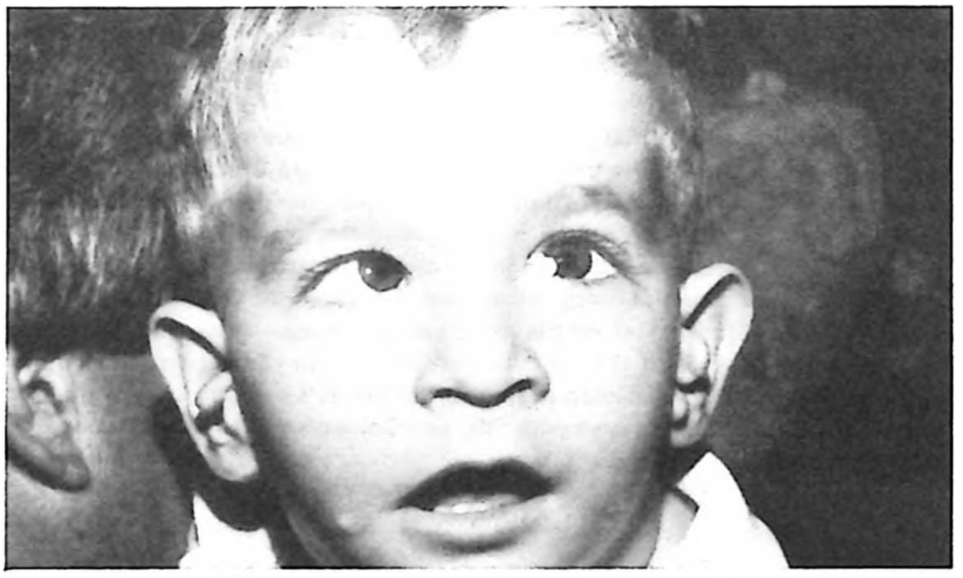

Fig. 1: Patient at 15 months. Note epibulbar dermoid in the left eye and bilateral preauricular appendages.

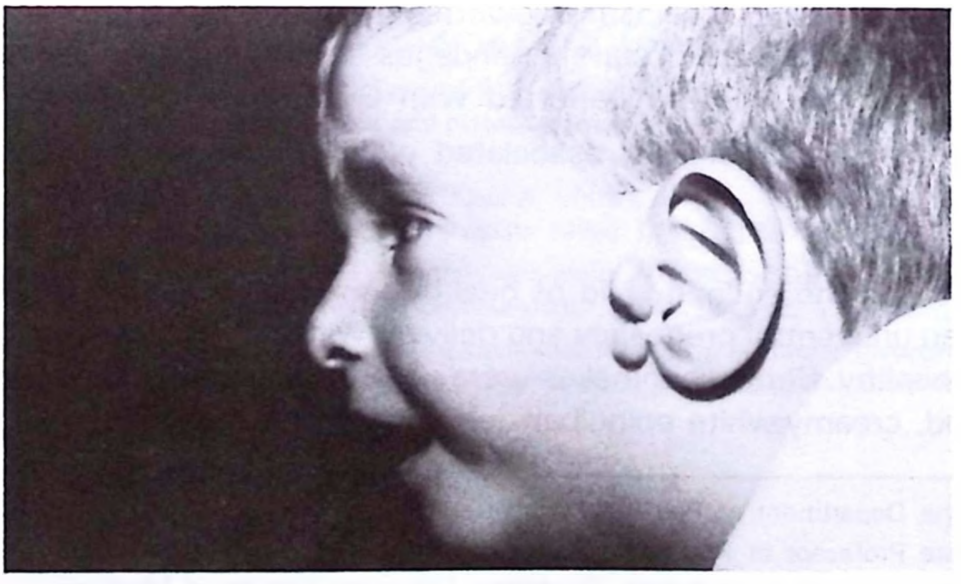

Fig. 2: The combination of malar hypoplasia and micrognathia gives the patient's profile a characteristic appearance.

34 mg/dl. Based on these clinical and biochemical findings, the diagnoses of phenylketonuria and Goldenhar's syndrome were made.

He was put on a low phenylalanine diet and benefitted from the dietary therapy. He was able to walk unaided when last seen at 18 months of age.

Discussion

Goldenhar's syndrome, described by Goldenhar in 1952[10], is characterized by epibulbar dermoids, preauricular appendages and pretragal fistulas. Preauricular appendages are one of the most consistent findings of the syndrome, with unilateral involvement usually being reported. But, there are numerous exceptions, including our case. Epibulbar dermoids and lipodermoids occur unilaterally in half of the patients with Goldenhar's syndrome. In our case, epibulbar dermoids were in the patient's left eye. Lipodermoids do not occur as frequently as do epibulbar dermoids, and were not found in this case. Several ocular and vertebral anomalies are described later that have not been reported in the original cases. Hydrocephalus, mental retardation, cardiovascular, kidney, parotid and parotid duct, urethral, rectal and oral abnormalities, inguinal hernias, hemangiomas, rectovaginal fistulas and clubfoot are other less-frequently associated defects[10-15]. Among these only mental retardation was found in our case, although it was not clear to what extent PKU had played a role in the development of developmental delay.

Several vertebral anomalies and bony defects of the skull were reported in more than 50 percent of the cases in the literature. Skull and vertebral X-rays did not reveal any abnormality in our case. However, the computerized tomography of the brain showed a lipoma in the corpus callosum and some calcifications of the falx cerebri. The calcifications of the falx cerebri were described in Mellor's case[11]. The phenotypical features of untreated PKU, including blond hair, very lightly pigmented skin and "musty" odor, were found on physical examination in our case. Since the serum phenylalanine level exceeded 20 mg/dl and the ferric chloride test was positive, there was no doubt about the diagnosis of classical PKU.

Goldenhar's syndrome is sporadic. No evidence of any hereditary pattern was found in any of the reported cases with the exception of Krause and Summitt's[16,17], who described the syndrome in the same family. In contrast, PKU is inherited autosomal recessively and is the most commonly seen metabolic disorder in Turkey. The incidence of PKU is 1/4370 in our country the highest among the reported surveys[18].

We cannot say whether these two conditions occurred together by chance or as a result of genetic linkage. The reporting of further cases will clarify the association.

Developmental delay or mental retardation is a component of several syndromes. If children with these syndromes are not screened for preventable causes of mental retardation, such as PKU and hypothyroidism, they will become more retarded. The purpose of the present report, therefore, was not only to document the simultaneous occurrence of two conditions, PKU and Goldenhar's syndrome, but also to emphasize that metabolic screening tests must cover all children, especially in countries like Turkey where the incidence of metabolic disease is high. The overlap of clinical symptoms may lead to a delay in the diagnosis of certain treatable diseases.

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