OCULAR INVOLVEMENT IN HOMOCYSTINURIA*

BY

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An increasing awareness of the importance of metabolic disorder in disease processes in the last few years has focused attention on those which Garrod (1923) termed "inborn errors of metabolism". Many of these are due to disordered amino-acid metabolism, and those of interest to ophthalmologists include cystinosis and the oculo-cerebro-renal syndrome (Lowe, Terrey, and MacLachlan, 1952). A condition more recently discovered involving the sulphur-containing amino-acid homocystine has been reported by Carson, Cusworth, Dent, Field, Neill, and Westall (1963), who described two mentally retarded siblings (brother and sister) who constantly excreted moderate amounts of l-homocystine in the urine. They showed liver involvement, progressive paraplegia, red mottling of the skin, fine dry hair, and ocular lesions. It is the purpose of this short paper to report the ocular findings in another case in more detail and to draw attention to this condition, since Carson and others considered that there was a possibility that the condition is not too rare, seven other cases having been already discovered.

The normal breakdown of methionine to cystine comprises:

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\text{Methionine} \rightarrow \text{Homocysteine} \rightarrow \text{Serine} \rightarrow \text{Cystathionine} \rightarrow \text{Homoserine} \rightarrow \text{Cysteine}
\]

The detailed mechanism of the error of metabolism, if such exists in homocystinuria, remains obscure. The first hypothesis of Carson and others, that there was a block in the normal conversion of methionine into cystine, has not been confirmed. An alternative theory is that the primary cause is a defect in methionine transport.

Case Report

A boy aged 5\(\frac{1}{2}\) years had been late in reaching each stage of development. He could not sit alone till 8\(\frac{1}{2}\) months, stand till 20 months, or walk till 26 months. When he did walk it was with a waddling broad-based gait. Speech was limited to unintelligible monosyllables. He was hyperkinetic and irritable. He was toilet-trained by day, but enuretic, and his urine had a strong ammoniacal odour. Attention was first called to his poor vision when he was 4 years old by the fact that he watched television with his nose almost touching the screen.

Examination.—The hair was sandy in colour and unusually fine and dry. Neurological examination revealed weakness of both flexion and extension of the hips and trunk. The ankle and knee reflexes were hypoactive. There were no other neurological abnormalities. The mental age and function were below that of an average 2-year-old child. X rays showed severe retardation of

* Received for publication February 26, 1964.
development of bone age. Liver biopsy revealed severe fatty infiltration. Urine examination revealed a quantity of homocystine. Metabolic studies showed intolerance to methionine. The child had an inguinal hernia, and an ocular examination was performed under general anaesthesia at the same time as the hernia was repaired.

**Ocular Findings.**—Both eyes were slightly microphthalmic. The sclerae were white and corneae bright and transparent. The anterior chambers were of irregular depth, being shallower infero-nasally. Both pupils were round and 3·5 mm. diameter; both had been noted to react normally to light before anaesthesia. The irides were pale blue and showed iridotension with movement of the child's head. Each crystalline lens was subluxed infero-nasally and showed a tendency to spheroptalmia, but with no visible opacities or colobomata. The fundi were normal in appearance. The ocular tension was 15 mm. Hg (Schiötz) in each eye.

Gonioscopy of the right eye revealed irido-corneal contact infero-nasally from 1 to 8 o'clock, but elsewhere the angle was normal in appearance and depth. In the left eye the angle showed some narrowing at 9 o'clock but was open all round.

Retinoscopy indicated a fairly high degree of myopia; right eye −10 D sph., −3 D cyl., axis 110°, left eye −10 D sph., −2 D cyl., axis 60°.

**Family History.**—A 2½-year-old female sibling, who likewise excretes homocystine, has similar neurological and ocular findings, although no attempt was made to perform an examination under anaesthesia since there is some suggestion that children suffering from this condition may hold a much higher anaesthetic risk. There are no other siblings nor any other family history or record of consanguinity.

**Comment**

A case is described of homocystinuria, a condition which has only recently been recognized, in which the presenting features were severe mental retardation, muscle weakness, microphthalmia, and infero-nasal subluxation of each lens. At the present time no relationship has been found between this condition and Marfan's syndrome, in which the finding that hydroxyproline is excreted in excess also favours the diagnosis of a defect in collagen metabolism. In homocystinuria, subluxation of the lens may indicate a failure of normal development of the zonule of Zinn due to deficiency of cystine; it is probable that the zonular fibres are of a collagenous nature (Pirie, 1962) and cystine is one of the constituents of collagen (Eastoe, 1955).

Homocystinuria is to be distinguished from cystinuria and cystinosis.

Cystinosis, inherited as an autosomal recessive, is characterized by dwarfism, acidosis, hypophosphataemia, renal glycosuria, and the accumulation of cystine crystals in many tissues, but notably in the cornea. Cystinuria, on the other hand, is of no ophthalmological interest.

**REFERENCES**


