The Turkish Journal of Pediatrics 1996; 38: 253-256

GYRATE ATROPHY OF THE CHOROID AND RETINA*

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SUMMARY: Hasanoğlu A, Biberoğlu G, Tümer L. (Department of Pediatrics, Gazi University Faculty of Medicine, Ankara, Turkey). Gyrate atrophy of the choroid and retina. Turk J Pediatr 1996; 38: 253-256.

Gyrate atrophy of the choroid and retina is characterized by autosomal recessive inheritance, progressive chorioretinal atrophy beginning in late childhood, and hyperornithinemia with ornithinuria caused by deficient ornithine aminotransferase activity. In this paper, four patients with gyrate atrophy are described. All patients had visual impairment, mental retardation, hyperornithinemia, hypolysinemia, ornithinuria and lysinuria. The first case had hypermetropic astigmatism in contrast to other reported gyrate atrophies.

These are the first reported cases from Turkey, but gyrate atrophy may not be rare in Turkey since the frequency of some other metabolic disorders has also been reported to be high. It is suggested that gyrate atrophy must be considered in all patients with chorioretinal atrophy. *Key words: gyrate atrophy, hyperornithinemia.*

Gyrate atrophy of the choroid and retina is a rare, autosomal-recessive inherited form of progressive chorioretinal degeneration beginning in late childhood[1-8]. A relationship between this disease and increased plasma ornithine levels was first reported in 1973, and then it was considered an inborn error of metabolism[7]. The major clinical feature is a slowly progressive loss of vision leading to blindness, usually by the fourth decade of life[1-6]. Myopia and decreased night vision are early symptoms, usually already present in childhood[1-6]. The earliest ophthalmologic finding is small, yellowish 'dots' in the midperiphery of the ocular fundus, which gradually enlarge to circular areas of chorioretinal degeneration. These lesions enlarge and extend toward the posterior pole of the fundus. This is associated with constriction of visual fields, usually in the second decade of life. Virtually all patients develop cataracts in the late second or third decade and need surgery[1-6].

More than 100 biochemically confirmed cases of gyrate atrophy have been reported[1]. Here we report four patients with gyrate atrophy, the first reported cases in our country.

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Case Reports

Case 1 (Y.Y.)

A 16-year-old girl was first referred at the age of 12 because of night blindness and decreased vision. A presumptive diagnosis of astigmatism was made, and she was not seen again until the age of 16. Her parents were consanguineous and her aunt was blind. When she was referred to us, examination revealed hypermetropic astigmatism and midperipheral chorio-retinal atrophy (Fig. 1). She also had mild mental retardation.

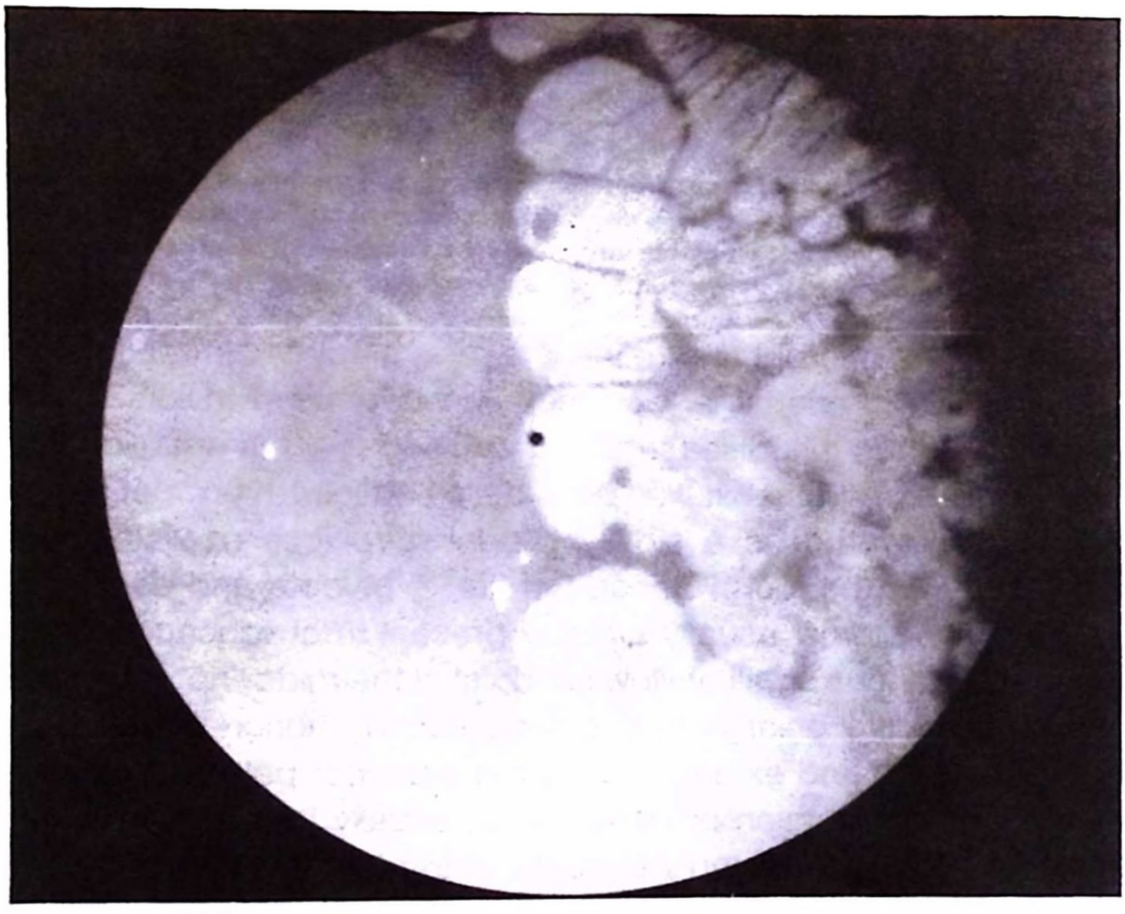

Fig. 1: Ophthalmoscopic examination of the first case.

On laboratory examination, serum ammonium, electroencephalography and electromyography findings were normal. Plasma ornithine levels were increased, and plasma lysine and arginine levels were decreased (Table I). Urine ornithine, lysine and arginine levels were increased (Fig. 2). Her mother's urine ornithine, lysine and arginine levels were also increased. Pyridoxine was administered to the patient at a dose of 500 mg/day.

Cases 2 and 3 (H.D., Y.D.) were siblings. They were 25 and 30 years old, respectively. Diagnosis was made by ophthalmoscopic examination, and hyperornithinemia was demonstrated with laboratory techniques (Table I).

A marked deficiency of ornithine amino transferase activity in cultured fibroblasts was demonstrated in the siblings.

Case 4 (G.H.) was a 21-year-old male whose visual symptoms started at the age of eight. He was also mentally retarded. On examination, bilateral myopy, cataract and peripheral chorioretinal atrophy was revealed. Laboratory evaluation confirmed hyperornithinemia and ornithinuria (Table I).

Table I: Plasma and Urine Ornithine and Lysine Concentrations of the Patients

	Plasma (mmol/dl)		Urine (mmol/dl)	
Patient	Ornithine	Lysine	Ornithine	Lysine
Y.Y.	44.3	7.10	1658.5	694.50
H.D.	32.6	2.40	1277.0	434.90
Y.D.	27.3	2.30	977.2	345.02
G.H.	33.5	4.33	1730.9	389.60
Control	7.5 ± 0.5	20.07 ± 09	18 ± 13	155 ± 114

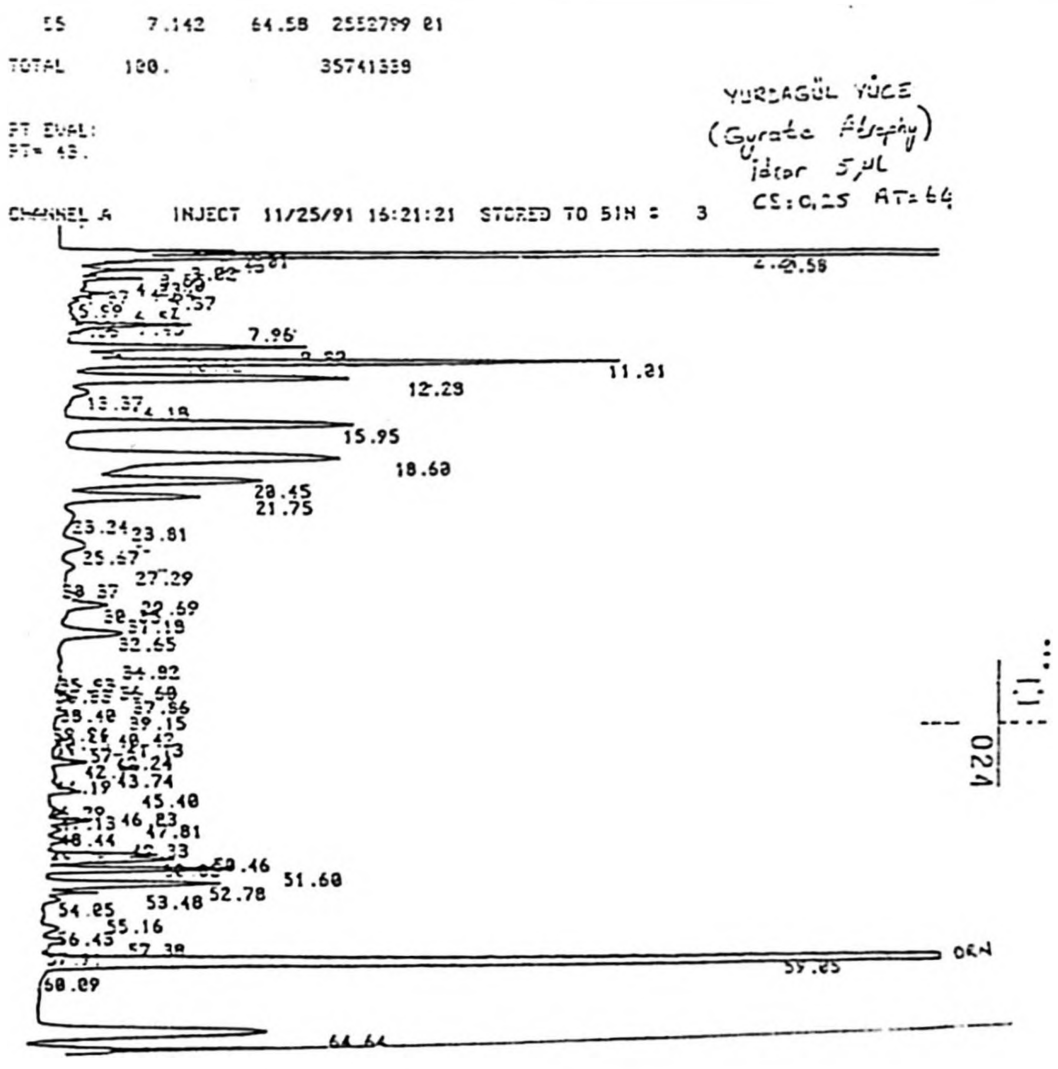

Fig. 2: Urine amino acid chromatography of the first case

Discussion

Gyrate atrophy has been a known entity since 1888, but the relation between this disease and increased plasma ornithine levels was first reported in 1973 by Simell and Tokhi[7]. The 10 to 20-fold increase in the plasma ornithine concentration is caused by deficient ornithine aminotransferase activity, which is the major enzyme that catabolizes ornithine[1,8]. Deficiency of this enzyme has been documented in cultured skin fibroblasts, phytohemagglutinin-stimulated lymphocytes, skeletal muscle cultures, hair roots and liver biopsy material[1]. This enzyme needs pyridoxal phosphate as a co-factor. In gyrate atrophy, along with hyperornithinemia there is hyperornithinuria, hypolysinemia and hyperlysinuria[1,8]. We observed ornithinuria, lysinuria and hypolysinemia in all of our patients.

Before visiual impairment, patients with gyrate atrophy are, for the most part, asymptomatic. The earliest symptoms are myopia and decreased night vision. Our first case had hypermetropic astigmatism in contrast to other published gyrate atrophies.

There are four general approaches for the treatment of patients[1,2]: stimulation of residual ornithine aminotransferase activity with pharmacologic doses of pyridoxine, correction of ornithine accumulation by reducing the intake of its precursor arginine and/or increasing renal ornithine losses, administration of creatinine and administration of proline.

In our first patient, restriction of protein intake and administration of pyridoxine at a dose of 500 mg/day was tried but failed to reduce plasma ornithine. Restriction of protein and administration of pyridoxine was also attempted in the other patients, but they could not be followed after diagnosis.

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