Rare disease

Gyrate atrophy of the choroid and retina with hyperornithinemia, cystinuria and lysinuria responsive to vitamin B₆

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Summary

In this report, an 8-year-old girl is presented with the complaint of progressive night blindness. The authors have performed eye funduscopy, which showed chorioretinal atrophy in gyrate shape. A high level of plasma ornithine was determined. Urinary excretion of ornithine as well as lysine and cystine were increased. Patient was treated with high dose pyridoxine supplement (500 mg/dl). The night blindness condition of the patient improved. After 1 month of pyridoxine therapy ornithine level of her plasma was successfully reduced and blindness improved.

BACKGROUND

Gyrate atrophy (GA) of the choroid and retina is a rare, autosomal recessive inherited disease causing progressive chorioretinal degeneration resulting in blindness. The primary defect is due to a deficiency of the enzyme ornithine Δ -aminotransferase, which is responsible for markedly elevated levels of ornithine in plasma and other body fluids.

CASE PRESENTATION

GA is a rare, autosomal recessive degenerative disease of the choroid and retina and is accompanied by defective ornithine metabolism.^{1–7} Simell and Takki² demonstrated the association with hyperornithinemia in 1973. The main metabolic features are those of hyperornithinemia and ornithuria caused by a deficiency of the mitochondrial matrix enzyme, ornithine aminotransferase. Ophthalmological features of the disease are myopia, night blindness, constricted visual field and complicated cataracts.^{8–9} We report a rare case of GA, in which the patient's high level of plasma ornithine, massive lysinuria and cystinuria was responsive to therapy with vitamin B₆ supplement.

INVESTIGATIONS

An 8-year-old girl is presented with the complaint of night blindness and visual loss during the past 3 years. She was the first child of healthy, consanguineous parents. She had no siblings. Her family history revealed that her parents were first-degree cousins and her grandfather had gradual visual loss that developed blindness at about age 50. Her refractive error measured -1.00 for the right eye and -0.75 for the left eye. Her best-corrected visual acuity was 3/10 in the right and left eye. Fundus examination of both eyes revealed sharply demarcated areas of choroid and retinal atrophy in gyrate shape and involving the midperiphery with the macular oedema (figure 1). Fundus fluorescein angiogram shows leakage from the left fovea, bilateral hyperfluorescence in macula-temporal area and cystoid

macular oedema (figure 2). Amino acid analysis revealed a high plasma ornithine level: 12.616 mg/dl with the normal range being 0.25–1.06 mg/dl. Urinary excretion of ornithine, as well as lysine and cystine increased. The level of those amino acids were as follows: ornithine: 3732.78 μ mol/24 h (normal: trace), lysine: 869.309 μ mol/24 h (normal: 64–642) and cystine: 82.309 μ mol/24 h (normal: 21–28). EEG showed diffuse slow activity. Her intelligence was normal.

OUTCOME AND FOLLOW-UP

Fundus examination and laboratory findings of our patient confirmed the diagnosis of GA of the choroid and retina with hyperornithinemia, cystinuria and lysinuria. A 2-week trial of pyridoxine therapy (300–600 mg/day) is recommended for all newly diagnosed patients to determine their responsiveness. Our patient was also treated with vitamin B₆ at a dose of 500 mg/day.

After 1 month, this vitamin supplementation successfully reduced her plasma ornithine level to nearly normal level (4.950 mg/dl) and urine ornithine level reduced by more than 50%–1226 μ mol/24 h. It was difficult to apply a natural low-protein diet to our patient. To delay the progression of the chorioretinal changes, UCD-2 (low arginine diet) was added to her normal diet.

Since arginine is the precursor of ornithine, providing a low arginine content special diet (UCD-2) makes sense. To increase discharge from kidneys, l-lysine and α -aminoisobutyric acid could be recommended. Also to remedy reduced plasma levels, additional proline and creatinine could be provided as support.

DISCUSSION

GA of the choroid and retina is a rare degenerative disease, characterised biochemically by a marked increase in blood ornithine levels, due to deficiency of ornithine Δ -aminotransferase.^{1–7} Chorioretinal dystrophy that

Figure 1 Fundus view of eye shows sharply demarcated areas of choroid and retinal atrophy in gyrate shape and involving the midperiphery with the macular oedema.

Figure 2 Fundus fluorescein angiogram shows leakage from the left fovea, bilateral hyperfluorescence in macula-temporal area and cystoid macular oedema.

begins in paediatric population (age range 0–16) often leads to blindness during the fourth to seventh decade of life.^{8 9} The mechanism of GA remains unknown; however, the adverse effects of creatinine or pyroline-5-carboxylate

deficiency on retinal function are thought to be a causative factor.¹⁰

The administration of pharmacologic doses of vitamin B₆ in a disorder caused by decreased activity of a B₆-dependent

enzyme is an established procedure.^{10 11} The disease is more prevalent in the Finnish population.¹² In the past, well over 150 cases of GA have been documented. Nearly 1/3 of these cases were from Finland and only seven of them (less than 5%) have been reported to be responsive to vitamin B₆ supplementation.¹³ Our patient is a rare case of GA, such that her plasma ornithine level decreased from 12.616 mg/dl to 4.950 mg/dl (nearly normal level: 0.25–1.06 mg/dl) after administration of 500-mg/day vitamin B₆ as dietary supplementation. The night blindness condition of the patient improved. Although several therapeutic regimens have been proposed; the reduction in ornithine accumulation obtained by reducing the intake of its precursor arginine (semi-synthetic low arginine diet) is the one most practiced.^{14 15}

We suspect that GA might be the reason for blindness in grandfather as well, because, it was reported that his blindness was started as 'night blindness', when he was in early age, similar to our current patient. Grandfather was living in a rural area village and passed away long before our patient reported to us, no further investigation was possible to make about grandfather. Accordingly, we suspect of

genetic link in GA, due to the occurrence of similar illness in the grandfather and granddaughter.

Competing interests None.

Patient consent Obtained.

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Learning points

- Child patients applying to doctor with night blindness complaint, could also be suspected for GA.
- When GA is observed, next step should be suspicion of ornithine metabolism disorder.
- To prevent blindness in adult population (age 40 and above), high dose vitamin B₆ treatment should be tried in all cases.
- To prevent ornithine build-up in the metabolism, a diet with low arginine level should be recommended.

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