LEBER'S HEREDITARY OPTIC ATROPHY: AN ATYPICAL CASE WITH RESPONSE TO HYDROXYCOBALAMINE THERAPY

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ABSTRACT

A 15-year old Chinese boy was diagnosed to have Leber's hereditary optic neuropathy (LHOA), having manifested with typical findings of bilateral severe visual loss and telangiectasia at the optic disc. However, no family history was elicited and an interval of more than 5 years separated visual loss in the two eyes. The latter is an extremely uncommon finding.

Visual improvement was rapid and marked after instituting intramuscular hydroxycobalamine 5 mg weekly. Bilateral improvement of Snellen acuity to 6/9 was achieved within 6 months. This is also unusual in that visual prognosis is generally poor in LHOA, although spontaneous remissions have occasionally been recorded. In addition, the eye with a longer history of poor vision responded to therapy first.

Keywords: Leber's optic neuropathy, optic atrophy, pseudo-papilloedema, hydroxycobalamine, Wolffe-Parkinson-White syndrome.

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INTRODUCTION

Leber's hereditary optic atrophy (LHOA) occurs typically in a young man between the age of 5 and 69 (often 15 to 30) with acute painless visual failure. This takes days to months and becomes bilateral within a year. Recovery is unusual and final acuities are often counting fingers. Inheritance is likely to be mitochondrial, with transmission from female carriers. No affected males have ever been documented to pass the disease to their children.

We report a case of LHOA in a patient with an unusually long interval between visual loss in the two eyes and who recovered on hydroxycobalamine therapy. This is the first time, to our knowledge that this time interval has exceeded 1 year.

CASE REPORT

Our patient, GST is a 15-year old Chinese student who noticed "shiny patches" in the centre of his right visual field of gradual onset in May 1988. Over the ensuing weeks, these separate patches coalesced to form a single large central visual defect. Although he reported a period of improvement at weeks, this was short-lived, and vision continued to deteriorate. The only other symptom during this period was slight nausea without vomiting or headache. There was no family history of visual loss, although he has four maternal uncles.

He was seen by an ophthalmologist 6 weeks after the onset of symptoms. Vision in the fellow eye was also noted to be poor before the age of 10 (unfortunately, the exact age of onset could not be determined). This had been attributed to developmental amblyopia. The CT scan, intravenous fluorescein angiography and ESR were found to be unremarkable. Oral prednisolone 60 mg/day had been tried for a week without success.

In July, GST was referred to the Neuro-ophthalmology Service of the National University Hospital. The Snellen acuity was counting fingers at 1.5 m in the right and counting fingers at 10 cm in the left.

Pupillary light reflexes were sluggish, with the left demonstrating a 1+ relative afferent defect. There was mild disc hyperemia and swelling in the right eye and temporal pallor in the left. In both eyes, telangiectatic dilatation of peri-papillary capillaries was evident. These did not demonstrate abnormal vascular permeability on fluorescein angiography. Similarly no disc staining typical of papilloedema was seen. Bilateral dense absolute central scotomas were documented on the Golman perimeter. Farnsworth D-15 testing showed dyschromatopsia with a red-green polarity.

No neurological abnormalities were found. However, a 12-lead electrocardiogram showed evidence of Wolffe-Parkinson-White Syndrome. The delta wave was directed inferiorly and anteriorly suggesting possibly a posterior tract more on the right side. 24-hour Holter monitoring fortunately did not reveal supraventricular tachycardia but only bouts of sinus tachycardia which were correlated with his palpitations. Propranolol 20 mg b.i.d. was instituted for these symptoms.

In September, he was started on I/M Hydroxycobalamine 5 mg twice weekly. The delay was due to slight difficulties in obtaining this form of vitamin B_{12} (as opposed to cyanocobalamine). 8 weeks later, vision in the left eye had improved to 6/60. At 12 weeks after the initiation of therapy, the left eye rapidly regained

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vision to the 6/60 line (the right could see 6/24 then). At the end of February 1989 (at 5 months), he was able to discern the 6/9 optotypes with both eyes.

In May, at the time of writing, Snellen acuity was 6/6 bilaterally. The appearance of the optic discs have remained unchanged. Humphrey automated static perimetry also documented steady improvement in his visual fields. He is currently doing well in school and plays an occasional game of basketball.

DISCUSSION

Our patient, one of the few Chinese reported in the literature, illustrates several fundamental points regarding LHOA as well as providing some thought-provoking new ones:

a) Diagnosis:
The fundus triad of telangiectasias, pseudo-papilloedema and absence of leakage or disc staining of fluorescein angiography is adequate criteria for the diagnosis of typical LHOA (1). A positive family history is not essential.

GST exemplifies the importance of careful examination of the disc with a direct ophthalmoscope to detect subtle pre and peri-papillary telangiectasia. This feature is unusual in papillitis and a correct diagnosis will save the patient from being drowned in systemic steroids especially when the disease becomes bilateral.

These vessels may be present from the age of 5 and are a useful genetic marker for the disease. Fortunately, none were detected in our patient's sibs. Careful follow-up is however warranted as they may increase in prominence with age.

Central scotomas and acquired red-green dyschromatopsias are also characterstic of LHOA. Careful perimetry and colour vision testing is mandatory.

(b) Natural history
There are also two "absolute" facts in the progression of this disorder –

1. It is INVARIABLY bilateral.
2. The second eye will be involved within ONE YEAR. There are few diseases in nature which follow such a strict biologic clock (1). Our case is one of the very few in the world literature (and perhaps the only Chinese) where the second eye was affected more than 5 years later.

Leber's beginning in children younger than 10 years of age is difficult too diagnose as birth trauma or other congenital defects can also cause poor vision. However, the recovery of our patient's first affected eye after the initiation of therapy confirms the diagnosis of LHOA.

(c) Associated cardiovascular abnormalities
Electrocardiograms should be performed on all cases of LHOA and their maternal family. Pre-excitation syndromes due to anomalous conduction bundles bypassing the A-V node are reported to found half of the female descendants (in the descending male line, they have the same incidence as a normal population).

The increased risk of systemic hypertension in these patients also warrants that they be observed carefully in their adult life.

(d) Recovery and treatment
It is often quoted that although spontaneous recovery is not uncommon, it is rarely excellent in both eyes and "invariably" the poorer eye before treatment remains so. Most cases which recover well have often received treatment within a year. On average, acuity only improves after a year, with another year needed to achieve best acuity.

GST improved in the eye which had been affected for more than 5 years. This improvement occurred within 2 months of beginning therapy and preceded that of the fellow eye. Within 1 year, almost full recovery had been achieved bilaterally.

Disturbed cyanide metabolism is a postulated pathophysiologic mechanism in LHOA and forms the basis for hydroxycobalamine therapy (2). Although we cannot be certain that we are helping patients with this treatment, we suggest that all patients with LHOA be given a therapeutic trial of at least a year. The pain of intramuscular injections is a small price to pay for permanent blindness.

In patients refractory to this regime, we would consider an exploratory craniotomy with lysis of any opticochiasmatic arachnoid adhesions as advocated by Imachi (3) and Miller (4). Although seldom practised outside of Japan, this treatment may prove helpful in the Chinese population. Absence of optic atrophy may be an added indication for this procedure.

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