PROGRESSIVE OPTIC ATROPHY ASSOCIATED WITH JUVENILE DIABETES MELLITUS : REPORT OF TWO CASES AMONG FIRST COUSINS

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ABSTRACT

Two first cousins both suffering from insulin dependent diabetes mellitus since early childhood developed progressive optic atrophy from the age of 5 and 9 years respectively. They had similar ophthamological features which include optic atrophy with cupping, paracentral scotomata, and total achromatopsia. One patient also had stunted growth, delayed puberty and psychiatric disorder. Neither had diabetes insipidus and deafness. It is suggested that they may be a variant of DIDMOAD (Diabetes Insipidus, Juvenile Diabetes Mellitus, Optic Atrophy, Deafness).

Keywords: *diabetes insipidus, juvenile diabetes mellitus, optic atrophy and deafness (DIDMOAD); insulin dependent diabetes mellitus (IDDM); intravenous urogram (IVU); morning dose (OM); evening dose (ON).*

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INTRODUCTION

The cases reported are first cousins, the fathers of the patients being brothers. Other family members do not have diabetes mellitus or optic atrophy. There was no history of consanguinity in the last three generations (Fig 1).

Patient 1

JLCH, Chinese, now aged 14 years. He first presented at the age of four, in 1983 with history of polyuria, polydipsia and weight loss; he was diagnosed to have insulin dependent diabetes mellitus. The diabetes was controlled with subcutaneous semilente insulin 5U om and 3U on.

He was subsequently seen at the department of ophthalmology in March 1987, four years later, with a history of progressive deterioration of vision of both eyes. The corrected visual acuity was 6/24 in each eye. The pupillary response was sluggish, but there was no afferent pupillary defect. The optic dics were slightly pale and cup/disc ratios were 0.7 in the right eye and 0.6 in the left eye. The intraocular pressures were within the normal range. There was no evidence of diabetic retinopathy. Colour vision tested with Farnsworth Munsell 100 hue test revealed severe dyschromatopsia with deficiency of all colour senses.

In September 1988, his best corrected visual acuity had decreased to 6/36 partial in both eyes. Visual fields tests with Goldmann perimetry and Humphrey automated perimetry revealed paracentral scotomata in each eye.

The cup/disc ratios had increased to 0.8 in the right eye and 0.7 in the left. Computerised tomography of the brain performed to exclude compressive lesion was normal.

In January 1989, his polyuria and polydipsia persisted and he was admitted for bronchial asthma and stabilisation of diabetes. Water deprivation test showed no evidence of diabetes insipidus, audiogram showed no high frequency loss and Luteinising Hormone Releasing Hormone and Thyrotropin Releasing Hormone Stimulation Tests were within normal limits. His insulin was adjusted to Insulotard 14U om and 7U on.

In September 1991, the diabetes was poorly controlled and insulin administration was irregular. His growth was stunted, his weight was in the 97th pecentile and height in the 30th pecentile. Puberty was delayed, there was no secondary sexual characteristics at the age of 14 years. The father noticed that the patient's emotion had become very labile and his moods changed rapidly.

In 1991, at age of 14 years, the visual acuity deteriorated further to 6/60 in the right eye and 6/120 in the left eye. Cup disc ratios were 0.9 in the right and 0.8 in the left with pale and thin neuro-retinal rims. The intraocular pressures were slightly raised: right - 22 mmHg and left - 21 mmHg. His refraction was: Right -5.50/DS, Left -5.00/-1.00 x 80.

Intravenous urogram showed bilateral hydronephrosis and hydroureter with no vesicoureteric reflux or rental calculi.

Patient 2

ELCH, a 20-year-old Chinese, was diagnosed to have juvenile diabetes mellitus at the age of 8 and has since been on insulin. He has been compliant with medication and the diabetes is well controlled. He was seen by an ophthalmologist in 1983 with a history of deterioration of vision for four years, one year after the onset of diabetes. The visual acuity then was 6/18 in the right, 6/24 in the left. Intraocular pressures were within normal limits. Colour vision tested with Farnsworth Munsell 100 hue test showed marked dyschromatopsia, there was no specific pattern of deficiency but all the colour senses were depressed. The optic discs were noted to be pale especially temporally (Fig 2) and pupillary response was sluggish. Ophthalmoscopy and fundal fluorescence angiography showed no evidence of diabetic retinopathy. Electroretinogram was normal.

He was followed up regularly for eight years, during which the visual acuity decreased gradually by two lines to 6/30 in the right and 6/60 in the left eye. The intraocular pressures remained within the normal range. Optic discs became diffusely pale with slight increase in cup/disc ratio to 0.6 in both eyes.

The automated perimetry detected some areas of paracentral field defect which on follow-up was found to be non progressive.

Audiography showed no evidence of high frequency loss.

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Fig 1 - Family tree of the two patients (first cousins)

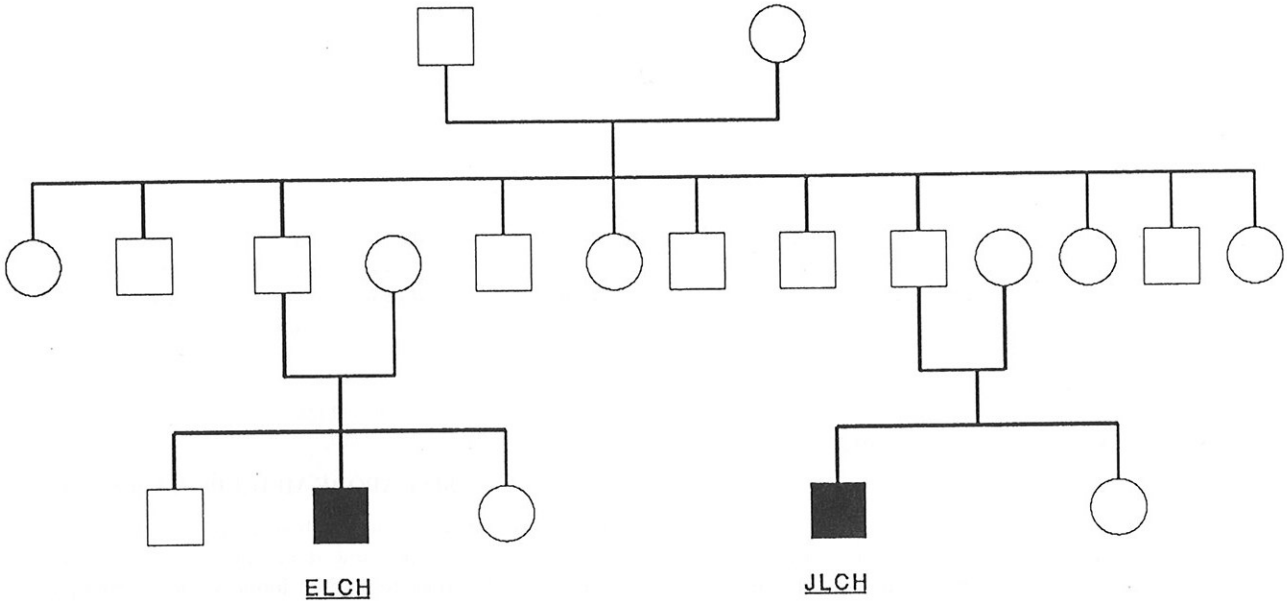
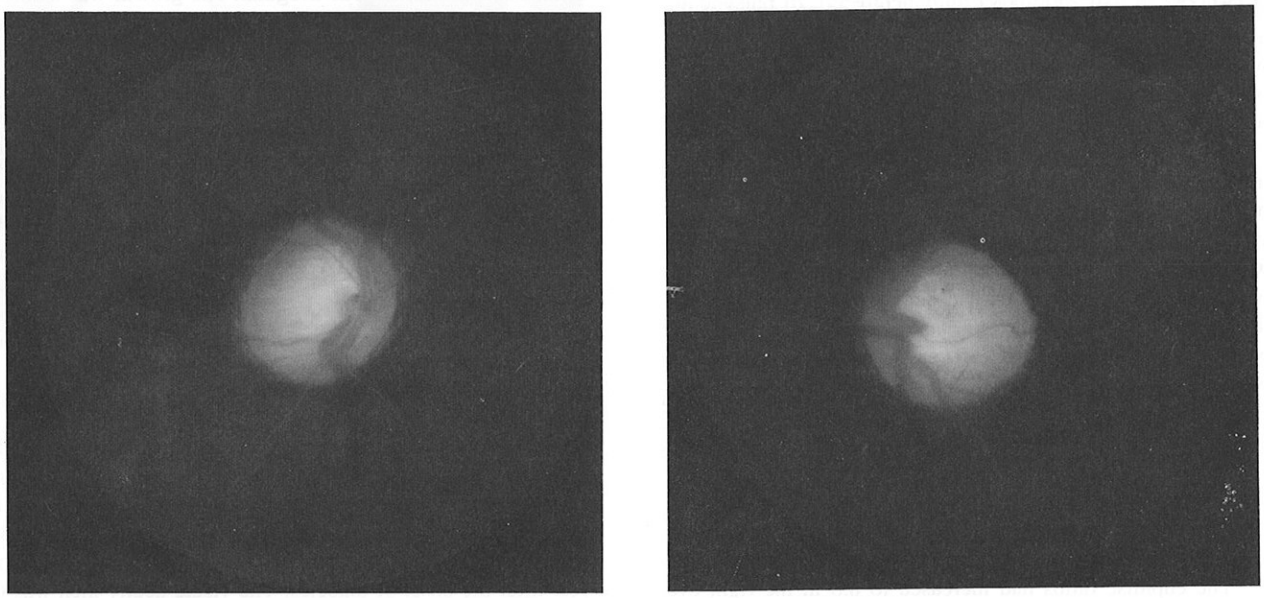


Fig 2 - Optic discs of patient 2



His stature was short but his intellectual, somatic and sexual development were normal.

Water deprivation test did not show diabetes insipidus.

Intravenous urogram only showed slight bladder retention of urine and no hydronephrosis or hydroureter.

DISCUSSION

Diabetes mellitus can affect the optic nerves in three ways: 1) Diabetic papillopathy, 2) Ischaemic optic neuropathy, and 3) Heredofamilial optic atrophy.

Diabetes papillopathy is a syndrome of juvenile diabetics characterised by transient bilateral oedema of the optic disc with minimal functional impairment. On examination, disc swelling ranges from mild oedema without haemorrhage to florid swelling with capillary telangiectasis, nerve fibre haemorrhages, exudate and cystoid macular oedema. It is a relatively benign condition which on occasion can result in visual deficit, but requires no specific intervention and represents a subgroup of anterior ischaemic optic neuropathy.

Ischaemic optic neuropathy of the nonarteritic form is commonly associated with diabetes mellitus. Both juvenile onset and adult onset can be affected, but the overall age of patients is lower than the arteritic anterior ischaemic optic neuropathy which usually affect the elderly. Anterior ischaemic optic neuropathy typically presents with sudden loss of vision, altitudinal visual field loss, and a swollen pale optic nerve head. The visual deficit is usually moderate and any improvement of vision is rare due to the subsequent development of optic atrophy.

Heredofamilial optic atrophy is a rare autosomal recessive syndrome. The association between juvenile diabetes mellitus and optic atrophy was first reported by Wolfram in 1938 of a family with two of four siblings with juvenile diabetes mellitus and optic atrophy. This has subsequently been reviewed extensively by Rose, Fraser, Friedman and Kohner[1].

Since then, many other case reports have described various associations with juvenile diabetes mellitus and the coexistence of optic atrophy: 1) perceptive deafness, 2) diabetes insipidus, 3) Friedreich's ataxia, 4) spina bifida occulta with frontal agenesis, 5) hydronephrosis, hydroureter, enlarged bladder, 6) Refsum's syndrome, 7) Alstrom syndrome[2-4], and 8) Laurance-Moon-Biedl syndrome.

The occurrence of juvenile diabetes mellitus and optic atrophy has been postulated by several authors to be an incomplete clinical manifestation of the DIDMOAD syndrome (juvenile diabetes mellitus, diabetes insipidus, optic atrophy and deafness)[2].

However, the rarity of the syndrome and our ignorance of the pathogenesis can only lead us to form certain hypotheses.

All available case reports (numbering about a hundred) suggest an autosomal recessive mode of inheritance in a large proportion of cases. This has been borne out by the observations that the DIDMOAD syndrome has not been reported in consecutive generations, the occurrence of the syndrome in several siblings of unaffected but closely related parents (consanguinous marriages) and the occurrence in one or two members in any affected generation[5].

However, such a autosomal recessive mode of inheritance would stress us greatly to explain the diverse clinical manifestations of the alleles involved.

Assuming that the inheritance is indeed autosomal recessive, all cases reports so far have yet to report any tests which have revealed the parents/siblings as having any features suggestive of a carrier state.

The constant association of juvenile diabetes mellitus and optic atrophy in these syndromes suggest that there may possibly be, yet some undiscovered genetic biochemical explanation for the syndrome and its associations.

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