HEREDITARY PRIMARY OPEN ANGLE GLAUCOMA: Case Study of a Nigerian Family

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SUMMARY

Objective: To present a case of hereditary primary open angle glaucoma in a Nigerian family.

Method: Six members of an Ibo family from Delta State, Nigeria were interviewed and examined by the authors. Information on age, gender, tribe, history of blindness, eye disease and other medical conditions was recorded. Visual acuity, slit lamp examination and gonioscopy, assessment of intraocular pressure using the pulsair non-contact tonometer and fundoscopy were carried out on the patients where indicated.

Results: The report of four generations of hereditary primary open angle glaucoma involving two males and two females is presented. At presentation, the patients were in the end stages of glaucoma with very poor vision – ranging from light perception to no light perception, high intraocular pressure of 31-48mmHg and cup disc ratio of 1.0 in both eyes at relatively young ages.

Conclusion: The mode of inheritance was most probably autosomal dominant. It is important to screen family members of patients with primary open angle glaucoma to reduce the problems that result from late presentation.

Key words: glaucoma, inheritance, family, autosomal dominant

INTRODUCTION

Basically, there is no precise definition of primary open-angle glaucoma (POAG). Probably the best that can be given, without making unwarranted assumptions, is to note that POAG is a characteristic form of optic neuropathy among patients with open angles that is related, to some degree, to the level of intraocular pressure.[1]

The possibility of genetic predisposition to glaucoma was first realized in 1842, when Benedict reported the occurrence of glaucoma in two sisters.[2] Since then, several studies have shown that family history is a significant risk factor for the development of POAG. Estimates of increased prevalence range from 2.8% to 13.5%.[3] The Baltimore Eye Survey showed that age-adjusted associations of POAG with a history of glaucoma were higher in siblings (odds ratio [OR] = 3.69) than in parents (OR =2.17) or children (OR = 1.12).[4] The odds ratios were slightly higher in blacks than in whites.

Most POAG pedigrees do not show a simple Mendelian pattern of inheritance.[5] An oligogenic, polygenic or multifactorial mechanism is usually proposed.[5,6] A minority of POAG pedigrees, however, do demonstrate a Mendelian pattern of inheritance. Several pedigrees of autosomal recessive inheritance have been described,[7-9] and it is said to be the commonest mode of Mendelian inheritance.[9] Fewer cases of autosomal dominant pedigrees have also been reported with a degree of penetrance varying from 60%-100%.[10,11] Extremely rare pedigrees showing possible sex-linked inheritance have been reported.[10]

This report presents four generations of hereditary primary open-angle glaucoma in a Nigerian family.

CASE REPORTS

Case 1

Case 1 is a 29-year-old male Ibo farmer from Delta State, Nigeria. He presented to the eye clinic on 15 March 2005 with a 3-year history of poor vision in both eyes. At the onset of visual loss, he experienced haloes around light. His vision has progressively deteriorated since then. There was no associated pain or redness. He had used some traditional herbal medication before presentation. There was no history of trauma to the eyes.

He is the first child in a monogamous family with six children: 3 males and 3 females. There is a family history of blindness in his mother, maternal grandfather and great grandmother. There was no other family history of blindness. He does not smoke or drink alcohol.

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At presentation, his visual acuity was light perception in both eyes. Intraocular pressure, measured with the pulsair non-contact tonometer, was 37mmHg in the right eye and 39mmHg in the left eye. His pupil was mid-dilated and poorly reactive to light. His optic discs were pathologically cupped and pale with a cup disc ratio of 1.0 in both eyes. Slit lamp examination did not reveal any abnormality. Gonioscopy with the Goldmann goniolens mounted on the Haag Streit slit lamp biomicroscope showed that the anterior chamber angles were open in all quadrants in both eyes. An impression of primary open-angle glaucoma was made.

Case 2

Case 2 is a 45-year-old Ibo farmer from Delta State, Nigeria, and is the mother of case 1. She presented with a history of poor vision in both eyes for 6 years and total loss of vision in the right eye for 1 year. There was a history of application of traditional herbal medication, which resulted in damage to the right eye a year before presentation.

There is a positive family history of blindness in the patient's father and paternal grandmother. She does not smoke or drink alcohol. She is not a known hypertensive or diabetic.

Her visual acuity was no light perception in the right eye and light perception in the left eye. There was a dense corneal opacity in the right eye while in the left eye, the cornea was transparent and the pupil was mid-dilated and minimally reactive to light. The optic disc was pathologically cupped with a cup disc ratio of 1.0. Intraocular pressure was 31mmHg in the right eye and 40mmHg in the left eye. Gonioscopy showed that the anterior chamber angle in the left eye was open in all quadrants. No abnormality was seen with the slit lamp biomicroscope.

An impression of right corneal opacity secondary to harmful traditional eye medication and primary open angle glaucoma was made.

Case 3

Case 3 is an 80-year-old male Ibo farmer from Delta State, Nigeria. He had a complaint of poor vision in both eyes over a 20-year period. There was no associated pain. He had used various traditional eye medications before presentation.

There was no history of trauma to either eye. There is a positive history of blindness in his mother, which occurred in middle age. She was already deceased at this time. There is no history of blindness among his siblings. He is not a known hypertensive or diabetic, and he does not smoke. He, however, takes alcohol occasionally.

His visual acuity was no light perception in both eyes. His pupils were mid-dilated and unreactive. There were lens opacities in both eyes. His optic discs were pale and pathologically cupped with cup disc ratios of 1.0 in both eyes. Intraocular pressure was 48mmHg in the right eye and 42mmHg in the left eye. Slit lamp examination did not reveal any cause of secondary glaucoma. His anterior chamber angles were open in all quadrants in both eyes.

An impression of primary open-angle glaucoma and bilateral immature cataract was made.

DISCUSSION

This report presented four generations of autosomal dominant primary open-angle glaucoma in a Nigerian family. The diagnosis of primary open-angle glaucoma was based on the complaints of painless visual loss, high intraocular pressure, open and normal appearing angles on gonioscopy, and the pathologically cupped optic discs. Visual field analysis could not be done because of the very poor vision in all the patients.

Only three generations of patients were actually examined: the index patient, his mother and maternal grandfather. The impression of primary open-angle glaucoma in the maternal great grandmother was presumptive. It was based on the history of blindness by middle age, somewhere between 40 and 50 years, and the fact that she was told that there was no cure for her condition at a hospital.

There is little doubt that some proportion of POAG has a direct genetic origin. This is well demonstrated by the many family pedigrees that have been published conforming to both recessive and dominant Mendelian inheritance models.[7-11] In this family study, only a few members who had no visual complaints could be examined. The father of case 1 was examined and his eyes were not glaucomatous. Two of his siblings were also examined (one male and one female) and their eyes were found to be normal. None of the uncles or aunties could be examined. They could not be convinced to make the trip from Delta State to Benin City to be examined when they did not have any visual complaints. The father of case 1 also denied any history of blindness or glaucoma in his own family.

A careful study of the pattern of inheritance of those affected shows that the most likely mode of inheritance was autosomal dominant. This is supported by the fact that glaucoma was expressed in consecutive generations even though the patients were married into families where there was no known history of blindness or a history suggestive of glaucoma. In these cases, intraocular pressure was typically high and seemed to occur at a relatively early age. Case 1 already had end-stage glaucoma at 29 years. In the case of the mother, grandfather and great grandmother, blindness had occurred by about the fifth decade of life. If we consider the fact that in POAG, by the time patients complain of significant visual loss, probably 10% or less of the axons remain,[1] then it is possible that glaucomatous damage may have started in most, if not all, of these patients

before the age of 30. This confirms an earlier report of autosomal dominant juvenile onset POAG,[12] characterized by onset before the age of 30 (often younger), a normal cornea, high intraocular pressure (30-50mmHg) with large diurnal variations and a poor response to medical therapy, necessitating early surgical intervention.[12]

Differences in severity or the age at which blindness occurred may be explained by the concept of variable penetrance and expression, which are phenomena associated with autosomal dominant inheritance. This further confirms that the mode of inheritance in this report is autosomal dominant. The absence of facilities for chromosomal analysis and genetic linkage analysis prevented further characterization of these patients.

Autosomal recessive inheritance is the more common type of hereditary glaucoma.[9] In this type, both spouses have a family history of glaucoma and then it is transmitted to their offspring. There was no such history in this report. Sex-linked inheritance is extremely rare,[10] and the pattern of inheritance in this report does not follow this pattern. X-linked recessive disorders only manifest clinically in males. In this report, case 2 and the great grandmother of case 1 are females.

The importance of genetics in glaucoma causation is exemplified by the discovery of the gene responsible for 1q linked glaucoma, which is the trabecular meshwork induced glucocorticoid response (TIGR) protein.[5] TIGR protein may cause increased intraocular pressure by the obstruction of aqueous outflow, which leads to glaucoma. The identification of the GLC1A, GLC1B, GLC1C and other future glaucoma genes has enormous clinical potential both for understanding the causation of glaucoma and gene therapy. This will reduce avoidable blindness from glaucoma.

The adjusted prevalence rate for POAG has been shown to be at least 4 to 5 times higher in blacks than in whites. It is suggested that this may reflect an underlying genetic susceptibility to both adult and juvenile onset POAG.[13] This emphasizes the importance of screening family members of patients with POAG.

CONCLUSION

This report has presented 4 generations of autosomal dominant primary open-angle glaucoma in a Nigerian family. The cases show that heredity could be a significant risk factor in the causation of primary open angle glaucoma and underlines the importance of screening for early detection of glaucoma, especially in a family that has a history of glaucoma. In this case, it was known that the maternal great grandmother of case 1 had an incurable cause of blindness, most likely glaucoma, but she was not told that it could be hereditary, neither were members of her family screened. If this had been done, glaucoma blindness would not have occurred in her offspring as it would have been detected early. Since it may not be practical to screen everybody, family members who are at high risk can be screened for early detection of glaucoma.

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