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Retinitis pigmentosa genetics: A study in Indian population

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Abstract

A total of 151 retinitis pigmentosa (RP) patients from 83 families were screened and the frequencies of different genetic categories studied. One hundred and ten patients out of 151 had a positive inheritance pattern, and autosomal recessive (AR) emerged as the predominant (53 out of 151), genetic pattern followed by isolated or sporadic (41 out of 151) cases. Further study of autosomal recessive cases revealed consanguinity as the main characteristic (49 out of 53) in the Indian population studied. Early onset and severe progression of disease was seen in the consanguineous group.

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Full Text

Retinitis pigmentosa (RP) is a progressive degenerative condition of the retina which eventually leads to blindness over a period of several years. It is a major cause of visual loss all over the world.[1][2][3][4][5][6][7]

Since the first report in 1662, several more have appeared regarding the genetic classification of RP patients.[8] Due to the various clinical presentations of patients belonging to different genetic classes,[9],[10] it becomes important to define the clinical subtypes occurring in each of the genetic classes along with the modes of inheritance.[11] This would also facilitate counselling.[12]

In this report, the genetic classification of the RP patients from India and their clinical subtypes have been described.

MATERIALS AND METHODS

A total of 151 patients from 83 families were examined. The patients showed all the symptoms of primary RP.[3],[7],[11],[13] Cases from different syndromes were excluded from the study. The study includes the data of RP patients listed from May 1991 to May 1993 at the Sathye Eye Hospital, Pune, India.

They covered a wide cross section of the Indian population namely from the states of Maharashtra, Karnataka, Tamilnadu, Kerala, Madhya Pradesh, Uttar Pradesh and Gujarat. The patients were chosen using the following criteria: (1) bilateral involvement (2) constriction of the visual field (3) progessive loss of vision (4) diminished or absent electroretinography (ERG) response, and (5) noisy P2 on visual evoked potential (VEP).[7],[11]

Retinal evaluation of these patients was carried out using binocular indirect ophthalmoscope which revealed various degrees of bone spicule pigmentation of the retina. Perimetry studies (Lister's perimeter) showed constriction of visual field. ERG and VEP were recorded on Nicolet Ganzfield [Nicolet compact 4]. Measurement of refraction, evaluation of visual acuity and slitlamp examination were carried out for all the patients.

The clinical subtypes defined is the modified form of those by Kaplan J. et al.[11]

1. Appearance of the symptoms (nyctalopia, constricted visual field) before the age of 15 were defined as early onset forms as against the late onset ones wherein the symptoms appeared later in adulthood.

2. Severe forms exhibited highly constricted fields of vision, diminished visual acuity before the age of 30 whereas mild forms had retained their visual acuity and had a moderately affected peripheral vision.

3. Senile forms were defined as the late onset form of the milder variety form of the disease.

Pedigree charts of the patients were tentatively established by recording the family history of each of the patients. As many family members as possible were examined by the clinician for the symptoms of RP. Exceptionally large families and those with deceased affected members posed some problems. The pedigrees were then confirmed. According to the mode of inheritance the patients were categorised into the following broad classes.[11],[14]

Autosomal dominant (AD): All subjects in this category showed vertical transmission of the disease for at least two generations. Unaffected members did not trasmit the trait to their offspring. Both males and females were at equal risk [Family A, [Figure:1]].

Autosomal recessive (AR): One or more subjects were affected from one sibship. Patients with parental consanguinity were included in this class [Family B, [Figure:1]].

X-Linked (XLRP): Subjects affected were males. Females were carriers. Vertical transmission of the trait for at least two generations was observed. Affected males did not transmit the disease to their offspring [Family C,[Figure:1]].

Male sibships (M sib): Males from the sibship were affected with no family history of the disease [Family D, [Figure:1]].

Genetically undetermined or inconclusive: The mode of inheritance could not be determined with certainty [Family E, [Figure:1]].

Sporadic or Isolated (ISO): This category included subjects with no known genetic history. A single individual was involved.

RESULTS

A total of 151 patients from 83 families from different parts of India were studied [Table:1]. Of these, 110 were found to have a positive family history and 41 were sporadic or isolated type. The predominant classes were two, AR and isolated types, constituting 53 and 41 out of 151 cases respectively. More than 92% (49/53) of the patients of AR category showed a positive history of consanguinity. This neccessitated further classification. Thus ARRP was subclassified into 1. Non-consanguineous and 2. Consanguineous, which were defined as follows:

1. AR non-consanguineous: This subclass included patients essentially from one sibship with no history of consanguinity in the family. Parents were normal on examination (family B1, Figure:2]).

2. AR consanguineous: This subclass further contained two types of pedigrees namely (a) AR (D) and (b) AR (R) depending on the presence or absence of the RP trait in the family prior to appearance of consanguinity.

a) AR (D): In this group, the presence of the RP trait prior to appearance of consanguinity in the family led to a pseudodominance of the trait in the family (family B2, [Figure:2]).

b) AR(R): In this group, the trait appeared only after consanguinity. Families with single as well as multiple consanguinities were included in this group (family B3' and B3", [Figure:2]).

Clinically the following observations were made regarding each class.

AR-Nonconsanguineous [Table:2a]: All the cases showed late onset of the disease. Early onset and senile forms were absent. The number of affected males as well as females was the same. Severe forms as well as mild forms were found. The number of patients was, however, less to draw significant conclusions.

AR Consanguineous- AR(D) [Table:2b]: The number of affected females was more than the number of males. Clinically maximum number of early onset severe cases were found (21/25) in this group. The onset was either congenital or within five years of life (early onset). These patients showed all the signs of advanced RP like profusely pigmented retina, field of vision < 10 degrees, visual acuity of counting fingers close to face or less. Other signs commonly seen in this group were bilateral cataract, reddish pigment on the macula, absence of ERG response and very noisy VEP. These patients also complained of intolerance to bright light, frequent headaches, giddiness and sudden flashes of light. Any type of stress or strain made them more symptomatic.

AR Consanguineous AR(R) [Table:2c]: Here, the early onset cases were maximum. Both severe as well as mild forms were observed. Congenital cases were absent and mean age of onset was 8 years. In early onset severe cases, symptoms of advanced RP such as severe loss of vision and formation of cataracts were not observed even after 15 years from the onset whereas in AR(D) these appeared within 10 years of onset.

Autosomal Dominant AD [Table:3]: Early onset case were more but no congenital cases were found. The average number of affected subjects per family was between 3 and 4. Clinically they showed all the signs of RP along with cataracts at advanced stages. Progress of the disease took 10-15 years.

X-Linked (XLRP) [Table:4]: Here mild forms were absent. In both early and late onset cases, only severe forms existed. Senile and congenital onset were not seen.

Male Sibships [Table:5]: Early onset mild forms and late onset severe forms were found.

Sporadic/Isolated [Table:6]: Both mild and severe forms of early as well as late onset were found unlike the other categories. The mild form was more common than the severe one. Senile onset was also seen.

DISCUSSION

The clinical and pedigree analysis of RP patients from various studies show that AR and isolated cases form the predominant mode of inheritance and occurence of this disease [Table:7][Table:8]. In our study, isolated cases were seen in 41/83 families and AR in 23/83 families. The number of individuals affected in AR families were 53 out of a total of 151 cases studied. In 9 out of 14 reports reviewed by us [Table:7][Table:8] AR was the predominant inheritance pattern seen. The exceptionally high percentages of AR cases reported by Amman et al (8) and Boughman (8) may be because isolated cases were included in this category. The variations in the prevelance of a genetic class in various studies is probably due to the method of classification, innate differences in the genetic pools of the study population and reliability of information obtained from the patients. We did encounter some difficulties in correctly establishing the pedigree in cases of exceptionally large families, in families with polygamy and in those with reportedly affected deceased family members where the nature of the disease could not be confirmed by the clinician.

Reports regarding the detailed clinical features of ARRP and XLRP have appeared in the literature.[15],[16] ARRP being the predominant form of RP in India, a thorough study was felt neccessary. More than 92%[49/53] of our patients in AR category had a positive history of consanguinity, which necessitated further classification into AR(D) and AR(R) types.

Clinically, patients with history of consanguinity in the family showed maximum number of early onset severe case.[32/53] Although the number of patients with AR nonconsanguineous pattern was too small, early and senile onset of disease was not seen. The patients of AR(D) type of inheritance had characteristic symptoms of headache, giddiness flashes of light and worsening of symptoms after any stress or strain. Similar observations have been reported by others in RP patients.[11],[17], [18],[19] This group of patients could have congenital onset of the disease and also generally developed cataracts, as opposed to AR(R) group where cataracts were a rarity and congenital cases were not seen. The autosomal dominant patients had slowly progressive disease taking over 10-15 years.[14] There were no congenital cases in this category.

Multiple mechanisms may be at work on pathogenesis of RP.[20] The molecular basis has been studied by different methods and numerous genes have been isolated in patients with RP.[21] The phenomenon of apoptosis has been applied to RP with considerable experimental proof.[22] Still this single process could not explain the different rates of degeneration in various forms of RP. The proper classification of both, clinical and genetic characteristics thus becomes important to elucidate the possible mechanisms of pathogenesis in this class of retinal disorders. We hope that our classification helps in obtaining genetically as well as clinically homogenous AR cases required for such studies.

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References

1 Boughman JA, Fishman GA. A genetic analysis of RP. Br J Ophthalmol 67(7):449-54, 1983.
2 Bundey S, Crews SJ. A study of Retinitis Pigmentosa in the city of Birmigham.I prevalence.J. Med.Genet 21:417-20,1984.
3 Berson EL. Electroretinographic findings in RP. Jap. J. Ophthalmol 31:327-48, 1987
4 Bennett ML, Sanderson GF. Gardner RJ. et al. J.Prevalence of RP in Otago and Southland. West J Med 155:388-99, 1991.
5 Puech B, Kostrubiece B'Hache Jc, Francois P.J. epidemiology and prevalence of hereditary retinal dystrophies in the Norther France Fr Ophthalmology 14:153-63, 1991.
6 Grondahl J. Tapetoretinal degeneration in four Norwegian countries II. Clin. Genet 29:17-23, 1986.
7 Marmor MF, Aguirre G, Arden G, et al. Reitinitis pigmentosa:asymposium on terminology and methods of examination. Ophthalmol 90:126-31,1983.
8 Marcelle J. On the heredity of Retinitis pigmentosa. Br J Ophthalmol 66:405-16, 1982.
9 Heckenlively JR, Yoser SL, Friedman LH, et al. Clinical findings and common symptoms in Retinitis pigmentosa. Am J Ophthalmol 105:504-11, 1988.
10 Bird AC. Clinical investigation of R.P. Aus. New Zeal. J Ophthalmol 16:189-98, 1988.
11 Kaplan J, Bonneau D, Fre'zal J. et al. Clinical and genetic heterogeneity in Retinitis pigmentosa. Hum. Genet 85:635-42,1990.
12 Seiff SR, Heckenlively JR, Pearlman JT. Assessing the risk of Retinitis pigmentosa with age of onset data. Am J Ophthalmol 94:38-43,1982.
13 Miller SJ. Parson's diseases of the eye. Churchill Livingstone 17th ed. 211-12,1984.
14 Fishman GA. Retinitis pigmentosa:genetics percentages. Arch. Ophthalmol 96:822-26.
15 Fishman GA, Alexander KR, Anderson RJ. Autosomaldominant Retinitis pigmentosa: a method of classification. Arch Ophthalmol 103:366-74, 1985.
16 Fishman GA, Farber MD. Derlacki DJ. X-linked Retinitis Pigmentosa: a profile of clinical findings. Arch Ophthalmol 1988, 106:369-75.
17 Foxman SG, Heckenlively JR, Bateman JB., et al. Classification of congenital and early onset RP. Arch Ophthalmo 103:1502-6,1985.
18 Gawande AA, Donovan WJ, Ginsburg AP, et al.Photoaversion in RP. Br J Ophthalmol 73:337-41, 1989.
19 Fishman G. A Retinitis Pigmentosa: visual loss. Arch Ophthalmol 96:1185-88, 1978.
20 Bird AC. Investigation of disease mechanisms in Retinitis pigmentosa. Ophthalmol Paediat Genet 13:57-66,1992.
21 Humphries P, Kenna P, Jane Farrar G. On the molecular genetics of Retinitis pigmentosa Sci 256:804-8, 1992.
22 Jones SE, Meerabux JMA, Yeats DA, et al. Analysis of differentially expressed genes in retinitis pigmentosa reinas - Altered expression of clusterin mRNA. FEBS Lett 300:279-282,1992.