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A Study of Chromosomes in 28 Cases with Congenital Ophthalmologic Diseases[1)]

By

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(With 2 Text-figures and 2 Tables)

To date, a wide variety of congenital disorders has been screened for chromosomal abnormality. In the field of ophthalmology, information is available on chromosome aberrations in patients with congenital ocular diseases, showing that certain clinical features are not always associated with specific chromosome abnormalities (Lele *et al.* 1965, Kobayashi and Shimada 1966). In these years we have been engaging in a chromosomal survey in patients with congenital ophthalmologic diseases in a hope to contribute to cytogenetics in this field. In the previous study ten ophthalmologic patients were chromosomally investigated without finding any abnormality (Ikeuchi and Makino 1966). The results of a chromosomal survey in 28 additional cases with allied diseases are presented in this article.

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Materials and Methods: Chromosome studies were carried out on the basis of short-term leucocyte cultures established from venous blood of patients. Chromosome slides were prepared according to the air-drying method of Rothfels and Siminovitch (1958) with a slight modification.

Results

Clinical cnd chromosomal findings in patients under study are given in Tables 1 and 2, respectively. It was shown that all the 28 patients studied were found to possess a normal chromosome number together with a normal sex-determining mechanism, 46, XX in females and 46, XY in males.

Worth recording are the facts that an unusually long Y chromosome was found in 8 male patients which corresponded in size to chromosomes of group 16–18, and further that one case (no. 26) had without exception an unusual chromosome

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Table 1. Clinical findings in 28 patients with congenital ophthalmologic diseases

Case no.	Age	Sex	Diagnosis or clinical feature
1	6y	M	Cryptophthalmus (r); microphthalmus (l); coloboma iridis (l).
2	25y	F	Microcornea (bilat); aniridia (bilat); nystagmus (bilat); congenital cataract (bilat).
3	16y	M	Congenital ptosis (bilat); nystagmus; amblyopia; epicanthus.
4	1y3m	M	Posterior synechia (bilat); congenital cataract (bilat); suspected Lowe's syndrome.
5	1y6m	M	Hallerman Streiff's syndrome: congenital cataract (bilat), nystagmus (bilat), bird face, hypotrichosis.
6	37y	F	Coats's disease: exudative retinopathy.
7	18y	M	Atopic cataract; atopic dermatitis.
8	28y	M	Myopia (bilat); retinochorioidal atrophy.
9[a]	66y	M	Myopia (bilat).
10[b]	19y	M	Myopia (bilat).
11	3y	F	Buphthalmus (bilat).
12	29y	M	Retinoblastoma (r).
13[c]	8y	M	Retinoblastoma (bilat).
14	6y	F	Nystagmus; suspected total colour blindness.
15	12y	M	Detachment of the retina (l).
16	37y	M	Zonular cataract (bilat).
17[d]	6y	M	Zonular cataract (bilat).
18[e]	8y	F	Zonular cataract (bilat).
19	15y	M	Duane's syndrome: retraction, deficient horizontal ocular motility; strabismus.
20[f]	45y	M	Strabismus.
21	16y	M	Laurence-Moon-Biedl's syndrome: retinal pigmentary dignegration, obesity, mental retardation, small penis.
22	33y	M	Duane's syndrome: retraction, deficient horizontal ocular motility; strabismus.
23	39y	M	Suspected retinal angiogliosis.
24	34y	F	Suspected retinal angiogliosis.
25	10y	M	Eosinophilic glanuloma: exophthalmus, orbital tumor.
26	11y	M	Suspected retinal angiogliosis.
27	39y	F	Sjörgren's syndrome: polyarthritis, dry eyes and month.
28	10y	F	Marfan's syndrome: arachnodactyly, dislocation of lens.

a and *b*: the father and the brother of case 8. *c*: the child of case 12. *d* and *e*: children of case 16. *f*: the father of case 19. y: year. m: month. F: female. M: male. r: right. l: left. bilat: bilateral.

apparently similar in size to chromosomes 4–5. It is characterized by an unusually elongated and weakly stained structure proximal to the centromeric region of the long arm (Figs. 1–4). Karyotype analysis based on several excellent metaphasic cells made it clear that one chromosome of group 6–X–12 was lacking, and that the members other than the abnormal chromosome were morphologically normal.

Table 2. Chromosomal findings in 28 cases under study

Case no.	Chromosome counts					No. of cells obs.	Chromosome constitution
	<45	45	46	47	>47		
1			15			15	46, XY
2			11			11	46, XX
3			14			14	46, XY
4		3	43			46	46, XY (long Y)
5			16			16	46, XY (long Y)
6		2	31	1		34	46, XX
7		1	12			13	46, XY
8			17			17	46, XY (long Y)
9[a]			18			18	46, XY (long Y)
10[b]		1	16			17	45, XY (long Y)
11		1	11			12	46, XX
12			19			19	46, XY (long Y)
13[c]			19			19	46, XY (long Y)
14			17			17	46, XX
15	1	1	21		1	24	46, XY
16		2	17			19	46, XY
17[d]		2	15			17	46, XY
18[e]			15			15	46, XX
19			12			12	46, XY (long Y)
20[f]		1	19			20	46, XY (long Y)
21			14			14	46, XY
22	1		16			17	46, XY
23			13			13	46, XY
24		1	14			15	46, XX
25			13			13	46, XY
26		1	18			19	46, XY (a group-C chromosome with a large secondary constriction)
27			15			15	46, XX
28		1	15			16	46, XX

Discussion

Within the past ten years, a large number of papers have been published on chromosome studies in a wide variety of congenital disorders. Cytogenetic studies in the field of ophthalmology has however been in less progression than in other medical fields.

Recently, Lele *et al.* (1965), studying the chromosomes of five patients of coloboma iridis together with other congenital anomalies, found in 2 cases of them a pericentric inversion in chromosome no. 1. The same chromsome anomaly was found in the mother of one of them, normal in phenotype. Edwards *et al.* (1961) studied the chromosomes in three cases with colobomata involving the chorioid or retina as well as the iris, but found no definite chromosome anomaly in them. Case no. 1 with coloboma iridis was found to have a normal chromosome complement without

any morphological abnormality. A similar feature was previously reported in two cases with coloboma of iris and chorioid by Ikeuchi and Makino (1966). Further investigation may be requested for the inquiry into the relationship of coloboma of the iris with the chromosomal abnormality.

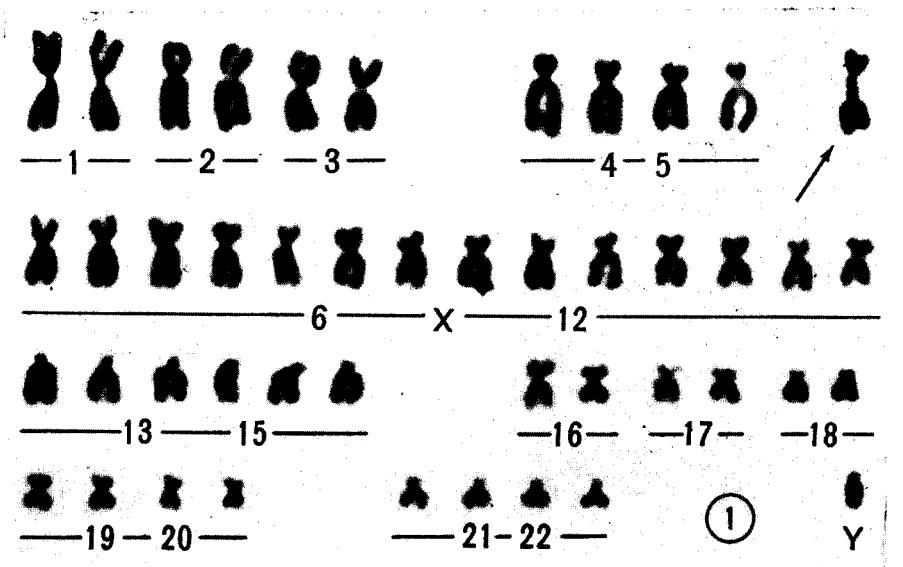
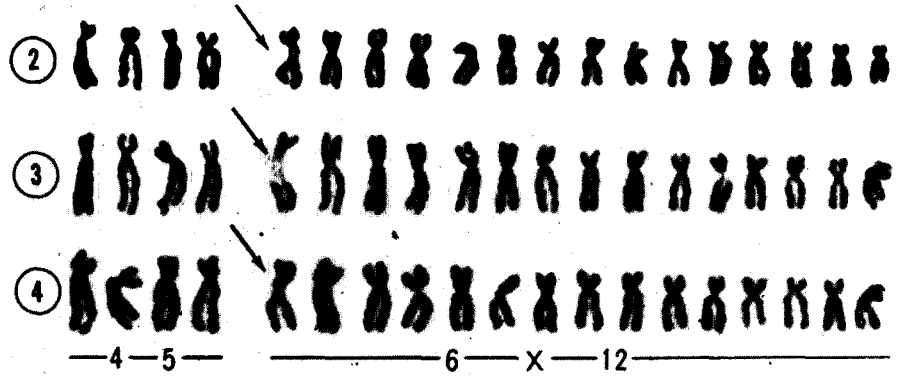


Fig. 1. Karyotype analysis of case 26 with suspected angiogliosis. The arrow indicates an unusual chromosome.

In two patients with Marfan's syndrome, Tjio *et al.* (1960) observed enlarged satellites in certain acrocentric chromosomes. Källén and Levan (1962) reported an abnormality in length of chromosomes 21 and 22 in the same syndrome. Makino (1964) described a normal chromosome complement in three patients of this syndrome. The present study also failed to detect any identifiable chromosome abnormality in a patient of this syndrome (no. 28). It is then possible to conclude that this syndrome is not always associated with certain chromosomal abnormality.

It is generally accepted that the unusual length of the Y chromosome is not necessarily associated with phenotypical anomaly in man. Recent report by Kato *et al.* (1965) merits special attention because of the fact that 8 cases out of 17 male patients with neuropsychiatric defects had an abnormality in size of the Y chromosome. In 20 male patients here under study, 9 cases were found to possess an unusually long Y chromosome. Four of them were relatives to the long Y chromosome carriers. At the present status of knowledge, no decided statement can be made that the relatively high incidence of the unusually long Y chromosome found in the present series is significant.

Of special interest is the fact that a case (no. 26) with suspected retinal angiogliosis had an anomalous chromosome characterized by an unusually elongated and weakly stained structure proximal to the centromeric region of the long arm. Most probable interpretation for the origin of the abnormal chromosome is that the secondary constriction of one of chromosomes 6–X–12 might be elongated due to unkown causes, resulting in an increase of length. In this connection, information has been obtained that certain chromosomes in group 6–X–12 have a distinct secondary constriction near the cetromere of the long arm (De la Chapelle 1961, Saksela and Moorhead 1962, Ferguson-Smith *et al.* 1962, Sasaki



Figs. 2–4. Partial karyotypes of groups 4–5 and 6–X–12 from the same patient as shown in Fig. 1.

and Makino 1963). A similar chromosome abnormality was found by Moores *et al.* (1966) to occur in a patient with a congenital heart disease. They noted the abnormal chromosome to be no. 9, suggesting no direct association between the marker chromosome and the congenital heart disease. In the present investigation, the said abnormality was found only in a patient (no. 26) with suspected retinal angiogliosis, whereas two other cases (nos. 23 and 24) with the same disease showed no such abnormality. Futher investigations now in progress have been going on the inheritability and genetic significance of this anomalous chromosome.

Summary

Chromosomes were studied in 28 cases with congenital ophthalmologic diseases. All of them were found to have a normal diploid number and a sex-determining mechanism. Nine male patients were found to possess an unusually long Y chromosome. One case with suspected retinal angiogliosis had an anomalous chromosome of group 6–X–12. It is characterized by an elongated and weakly stained structure near the centromeric region of the long arm.

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