

Chromosomal Aberrations in Epilepsy: An Analysis of 30 Cases.

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Abstract

- Background:** Chromosomal constitution of epileptics was studied in 30 cases out of which 19 were on treatment with antiepileptic drugs (63.3 %). The family history was positive in 46.7 % & 2 cases were mentally retarded.
- Results:** 5 treated cases showed chromosomal aberrations in the form of mosaic polyploidy, dicentric chromosomes, chromatid break & chromatid fragments. One untreated case also showed mosaic polyploidy.
- Discussion:** Mosaic polyploidy has been observed in both treated and untreated cases, so it is probably due to epileptic state itself. However the chromosomal damage in the form of dicentric chromosomes, chromatid breaks & chromatid fragments is seen in treated cases only; it is likely to be due to the effect of antiepileptic drugs.
- Conclusion:** Chromosomal aberrations in epilepsy are seen in a substantial number of patients. These may be due to epileptic state as such, effect of antiepileptic drugs or other undefined reasons.

Introduction

The incidence of epilepsy varies from 0.9% to 4% (1, 2). Familial tendency is common and it is expected that some chromosomal abnormality must be there in epilepsy especially in cases with positive family history. The present study aimed at finding out chromosomal constitution of epileptics including those having positive family history.

Materials and Methods

Epilepsy cases were selected out of patients coming to OPD (out patients department), emergency & EEG clinic of Government Medical College / Rajindra Hospital, Patiala from May 1989 to April 1990. Chromosomal studies were done in patients with no secondary cause of epilepsy and no clinical syndrome with known chromosomal aberrations e.g. Down's syndrome. 5 ml of venous blood was taken in a sample tube having 0.05ml of heparin as anticoagulant. Samples were analyzed in cytogenetic laboratory of Human Biology Department of Punjabi

University Patiala. The lymphocyte cultures were set up using modified Moorhead technique. After 72 hours cultures were harvested. G-banding of chromosomes was done by Seabright technique. Analysis of metaphase chromosomes was done by scanning the slides and 20 - 25 intact metaphases were selected for further analysis.

The selected metaphases were examined through Zeiss microscope (under 100X using oil immersion). In cases where chromosomal abnormality was found, 10 - 15 more metaphases were selected and examined. After microscopic analysis, 2 - 5 metaphases were selected for photography.

Results

30 cases of epilepsy were taken for chromosomal analysis. Patients were divided into five age groups as shown in Table 1 & 2. 19 patients were on treatment with antiepileptic drugs (63.3%) while 11 were not on any treatment (36.7%).

Family History of Seizures

The family history was positive in 46.7 % of patients i.e. 14 out of 30 cases (Table 3). These patients had at least one or more epileptic in family (Table 4). 3 patients had 2 more epileptics and 6 patients had 5 more epileptics in family.

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Received: 24.04.16

Accepted: 20.05.17

Table 1: Distribution of cases of epilepsy according to age

Age group (in years)	No. of cases	Percentage
5 - 14	7	23.4
15 - 24	10	33.3
25 - 34	7	23.4
25 - 44	2	6.6
45 & >	4	13.3

Table 2: Distribution of cases of epilepsy according to sex

Sex	No. of cases	Percentage
Male	18	60
Female	12	40

Table 3: Family history of seizures

Family history	No. of cases	Percentage
Positive	14	46.7
Negative	16	53.3

Table 4: Number of epileptics in the family

Sr. No.	Number of epileptics in the family other than patient	No of families
1.	1	5
2.	2	3
3.	3	0
4.	4	0
5.	5	6
Total		14

Table 5: Chromosomal aberrations, drugs used & duration of treatment

Sr. No.	Sex	Drugs used	Duration of therapy in years	Chromosomal aberrations
1	Male	Valproic acid & Carbamazepine	3.5	46, XY/46, XY, Chromatid break
2	Male	Untreated	-	46, XY/Polyploidy
3	Female	Phenytoin sodium	15.0	46, XX/46, XX, Dicentric chromosomes
4	Male	Phenobarbitone	6.0	46, XY/46, XY, Chromatid fragment
5	Male	Phenytoin sodium	15.0	46, XY/46, XY, Chromatid fragment
6	Female	Phenytoin sodium	3.0	46, XX/Polyploidy

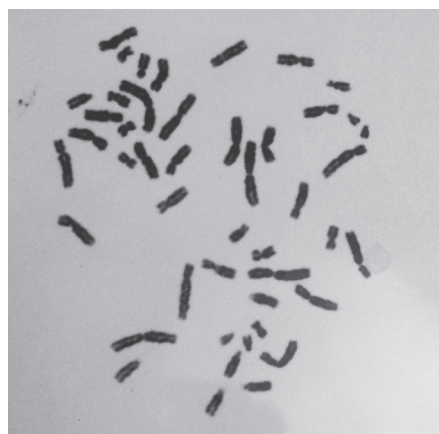


Fig. 1: Metaphase showing normal conventional chromosomes 46 XX

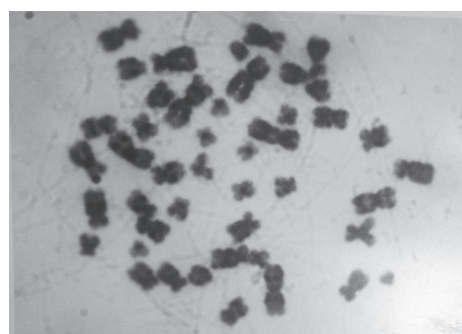


Fig. 2: Metaphase showing normal banded chromosomes & karyotype 46 XX

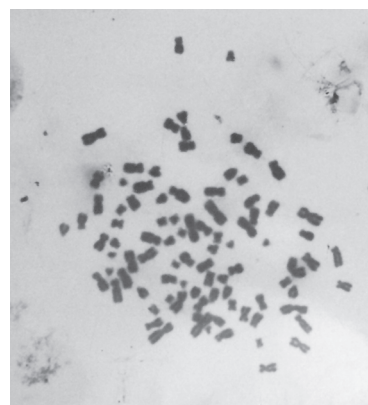


Fig. 3: Metaphase showing polyploidy

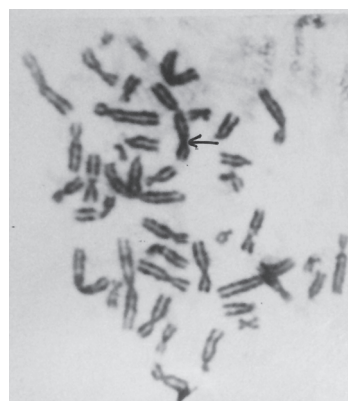


Fig. 4: Metaphase showing dicentric chromosomes

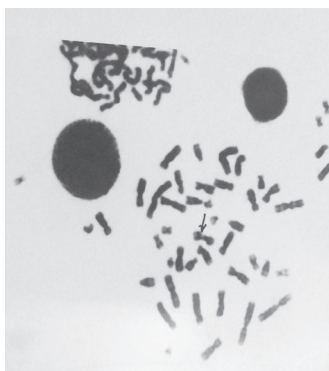


Fig. 5: Metaphase showing chromatid break

Mental Status & Epilepsy

2 patients were mentally retarded. One patient was 24 years old male with 3 years history of epilepsy, being treated with phenobarbitone and valproic acid since 3 years. Other was 45 years female with epilepsy since 15 years, on phenobarbitone since 3 years.

Cytogenetic Abnormalities

Out of 19 treated cases, 5 (26.3%) showed chromosomal aberrations in the form of chromosomal damage & mosaic polyploidy (Fig. 1 to 5 and Table 5). Chromosomal damage occurred in the form of dicentric chromosomes (one case), chromatid break (1 case) & chromatid fragments (2 cases). Mosaic polyploidy was seen in one case taking dilantin since 3 years. The patient with dicentric chromosomes was taking dilantin since 15 years, chromatid break was seen in the patient taking valproic acid and carbamazepine since 3.5 years. One patient of chromatid fragments was on phenobarbitone since 6 years and the other was on dilantin since 15 years.

Out of 11 untreated cases one showed chromosomal aberration in the form of mosaic polyploidy. Thus mosaic polyploidy was seen in both treated and untreated cases while dicentric chromosomes, chromatid breaks & chromatid fragments were seen in treated patients only.

Discussion

The present study has very high percentage (46.7%) of positive family history that too with 5 or more family members being epileptic in 6 patients. This is higher than the reported literature [3]. It may be due to selection bias or geographical variations. In the present study 2 cases (6.66%) showed mental retardation. This can be due to epileptic state itself or mental dulling effect of antiepileptic drugs.

Mosaic polyploidy has been observed in both treated (1 out of 19) and untreated (1 out of 11) cases. So it is probably due to epileptic state itself. However the chromosomal damage in the form of dicentric chromosomes (1 case), chromatid breaks (1 case) & chromatid fragments (2 cases) is seen in treated cases

only; so it is likely to be due to the effect of antiepileptic drugs. Antiepileptic drugs used by patients in the present study included valproic acid, carbamazepine, phenytoin sodium & phenobarbitone (Table 5, Sr No. 1 to 6). Chromosomal damage has earlier been reported with Carbamazepine & Phenytoin sodium by some investigators [4, 5]. However other studies have failed to show any chromosomal damage with antiepileptic drugs [6- 8]. Whether chromosomal damage is due to epileptic state as such or due to teratogenic effect of drugs remains unclear [4].

Conclusion

Chromosomal aberrations in epilepsy are seen in a substantial number of patients (6 out of 30, 20% in the present study). These may be due to epileptic state as such, effect of antiepileptic drugs or other undefined reasons. More studies involving a larger patient population are required to fully define this area.

Limitation

There is a time delay in publication of this manuscript.

Conflict of interest:	All authors declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
Funding:	No external funding
Guarantor:	Dr Devinder Singh Sandhu will act as guarantor of this article on behalf of all co-authors.

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